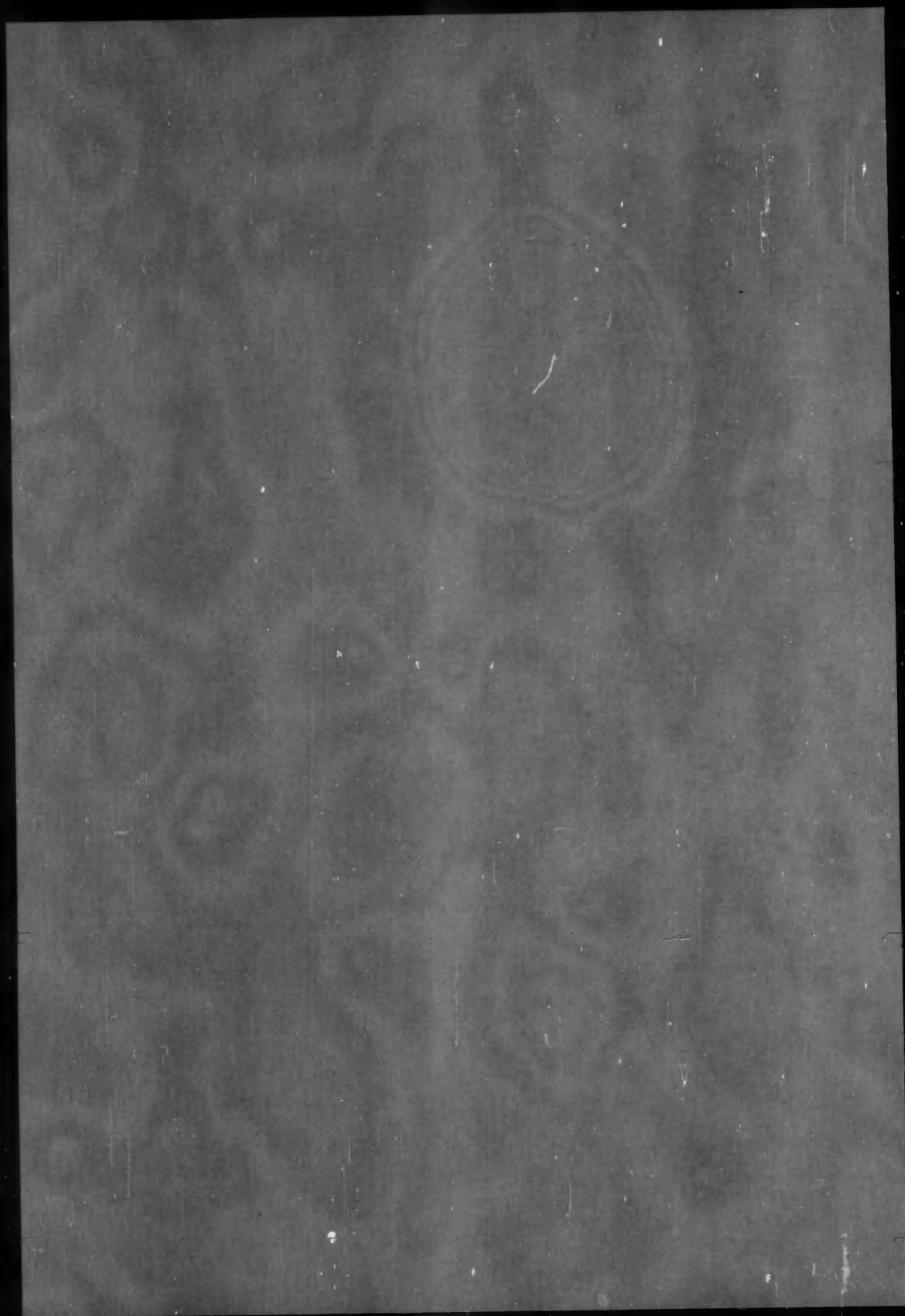


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No. 12

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1. Vander Veer, A. H., and Reese, H. H. *Am. J. Psychiat.*, 95:271, Sept. 1938.
2. Hess, W. R. *Diencephalon*. New York: Grune & Stratton, 1954.

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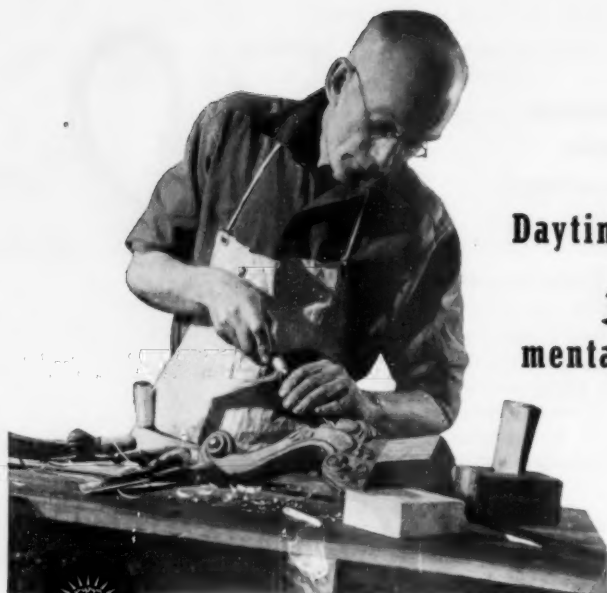
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1. Noco, R. H., Williams, D. B., and Rapaport, W.: J. A. M. A.: 156:821 (Oct.) 1954.



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1. Greenstein, L., and Sapirstein, M. R.: *A. M. A. Arch. Neurol. & Psychiat.* 70:469 (Oct.) 1953. • 2. Smith, B., and Forster, F. M.: *Neurology* 4:137 (Feb.) 1954. • 3. Smith, B. H., and McNaughton, F. L.: *Canad. M. A. J.* 68:464 (May) 1953. • 4. Whitty, C. W. M.: *Brit. M. J.* 2:540 (Sept. 5) 1953. • 5. Doyle, P. J., and Livingston, S.: *J. Pediat.* 42:413 (Oct.) 1953. • 6. Timberlake, W. H., Abbott, J. A., and Schwab, R. S.: *New England J. Med.* 252:304 (Feb. 24) 1955.

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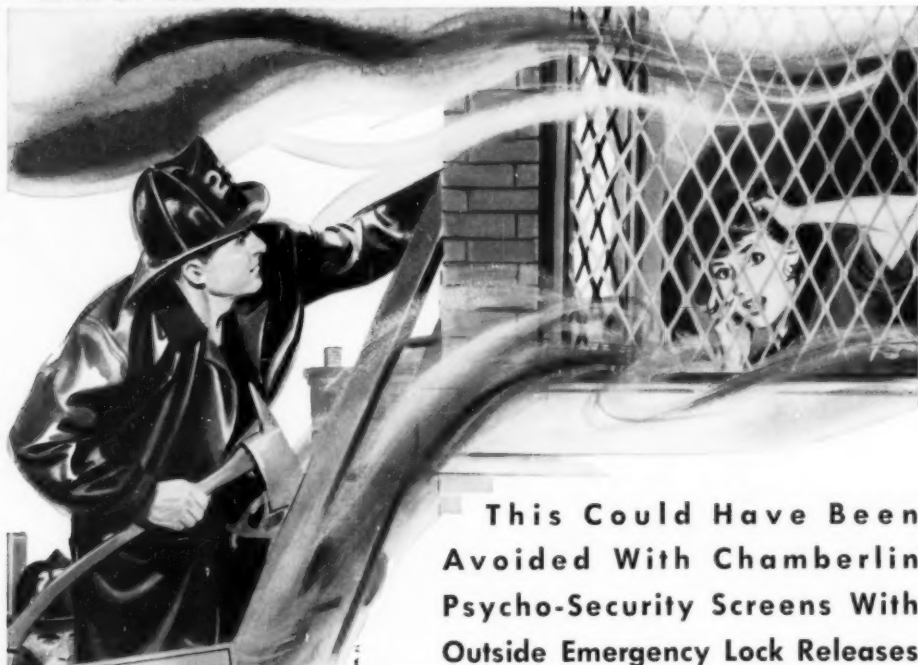
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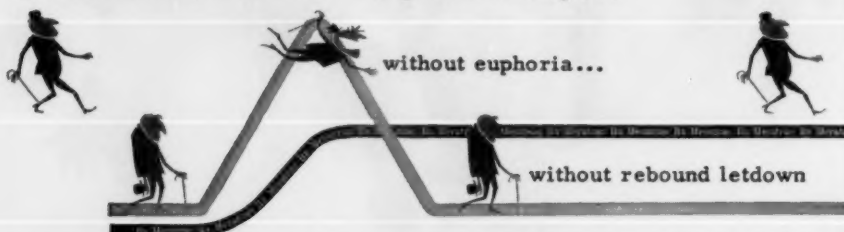
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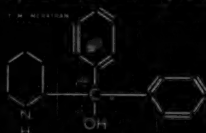
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1. Heath, R. C.: Discussion of power by Howard D. Fabing (alpha-(2-piperidyl) benzhydrol hydrochloride, a new central stimulant in the treatment of dyspareunia, spasmodic torticollis and choreoathetosis) presented before the American Neurological Association, Atlantic City, June 14, 1954. 2. Fabing, H. D., Hawkins, J. R., Moulton, J. A.: Clinical studies on alpha-(2-piperidyl) benzhydrol hydrochloride, a new antidepressant drug. Presented before the American Psychiatric Association, St. Louis, Missouri, May 2, 1954. 3. Fabing, H. D.: Alpha-(2-piperidyl) benzhydrol hydrochloride, a new central stimulant, in the treatment of dyspareunia, spasmodic torticollis and choreoathetosis, preliminary report (Merrell Picture Demonstration), American Neurological Association, June 14, 1954. 4. Himmelfarb, H. E.: Discussion of power (reference 2), American Psychiatric Association, May 2, 1954.

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1. Noce, R. H., Williams, D. B., and Rapaport, W.: J.A.M.A. 156:821 (Oct.) 1954.

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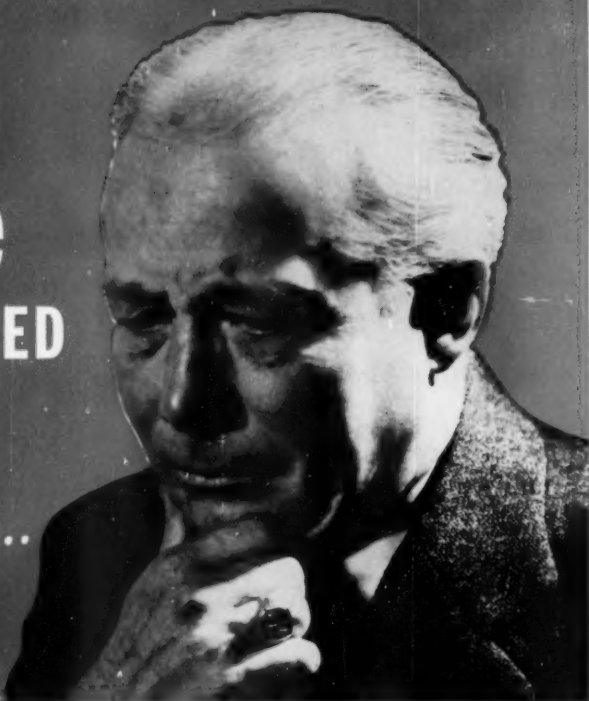
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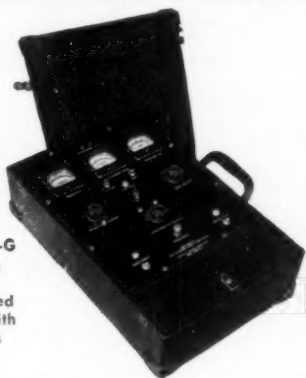
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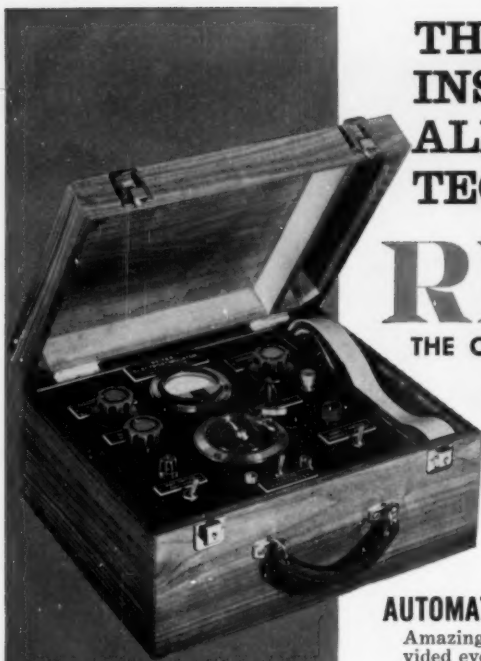
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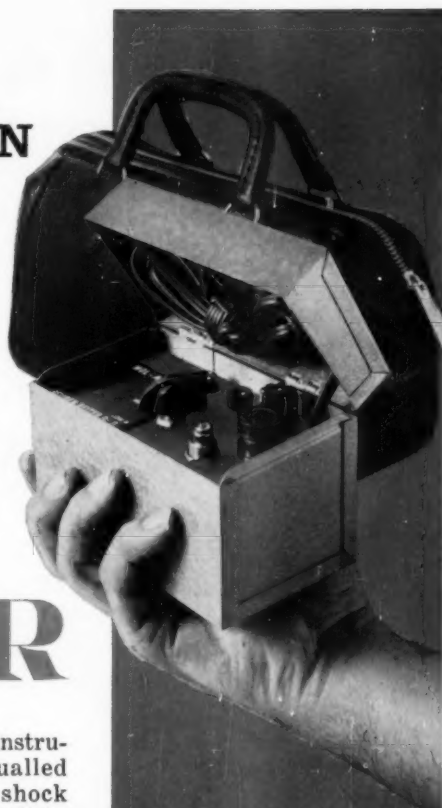
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EXPERIMENTAL PSYCHIATRY II^{1, 2}

CLINICAL AND PHYSIO-CHEMICAL OBSERVATIONS IN EXPERIMENTAL PSYCHOSIS

MAX RINKEL, M.D., ROBERT W. HYDE, M.D., HARRY C. SOLOMON, M.D.,
AND HUDSON HOAGLAND, Ph.D., Sc.D.
BOSTON, MASS.

INTRODUCTION

It is obvious that psychiatry would make progress with a procedure that would allow for the experimental reproduction of mental conditions. The advances in carbon-chemistry provided the means for the experimental approach to this problem. The fundamental discoveries by Otto Loevi and W. B. Cannon and their associates of the chemical transmission of nerve impulses and the relationships of the adrenalin system to emotional manifestations offered the scientific foundation. Of the chemicals used in the past, mescaline was more extensively investigated.

In 1930, H. de Jong⁽¹⁾ published a paper on mescaline-catatonia and the experimental production of dementia praecox symptoms. He administered mescaline to animals (especially monkeys) and humans and produced in them autonomic, motoric, and psychomotor phenomena, a triad of symptoms which he recognized as "principle of dementia praecox." Since then, other research groups, here and abroad, have used mescaline to study its mental effects, which have been described as similar to phenomena which occur in schizophrenia and other psychoses. In 1943, the Swiss chemist, A. Hoffman^(40, 42) accidentally discovered that the diethylamide of d-lysergic acid (LSD) produced interesting mental symptoms, and W. A. Stoll^(43, 44), confirming this observation, reported that mere traces of this chemical caused a temporary psychotic condition. It was evident that this chemical might offer a new tool for the experimental approach in

psychiatry. Rinkel, in 1949, obtained this chemical through the courtesy of Professor E. Rothlin, of the Sandoz Chemical Works in Basel, Switzerland, and together with DeShon, ventured into the field of experimental psychiatry.

LITERATURE

Many publications have since appeared relative to the chemical constitution of LSD and its physiological and psychological effects. Our experiences with the temporary psychosis-producing effect of LSD in humans were first reported by Rinkel⁽³⁵⁾ at the annual meeting of The American Psychiatric Association in 1950, and in subsequent publications in *The Psychiatric Quarterly*⁽²⁾ and *THE AMERICAN JOURNAL OF PSYCHIATRY*⁽³⁶⁾. Our work went on independently and unaware of other groups^(18, 27), working on a similar problem at about the same time, but using especially mescaline. The chemical and potency difference between mescaline and LSD is considerable.

Mescaline is a tri-methoxy-phenyl-ethyl-amide, and LSD is the diethylamide of d-lysergic acid:

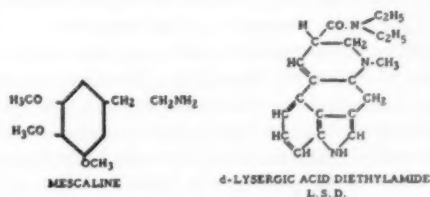


FIG. 1.

With mescaline, doses of as much as 500-1000 milligrams are needed to produce mental changes; of LSD, mere traces as small as 1 to $\frac{1}{2}$ microgram per kilogram body weight, or less, are sufficient to produce mental alterations.

¹ Read at the 110th annual meeting of The American Psychiatric Association, St. Louis, Mo., May 3-7, 1954.

² From the Department of Psychiatry, Harvard Medical School, and the Boston Psychopathic Hospital; Dr. Harry C. Solomon, Director; and the Worcester Foundation for Experimental Biology. Aided by a grant from the McCurdy Company, Rochester, N. Y.

PROCEDURE, METHODS AND CONTROLS

More than 100 normal males and females volunteered for our experiments. The extremely careful selection of subjects was the beginning of our controlled experimental design. The volunteers were first interviewed to establish their pre-experimental personality traits, which were of importance in the evaluation of their reactions, and to exclude persons who already were in a prepsychotic state, or to eliminate other risks. It was further of importance to know the volunteer's motivation for the experiment because this could intrinsically influence the outcome of the experiment. The following motivations were most common: Many wanted to have a temporary psychotic experience in order to approach an understanding of the feeling of a mental patient; others hoped to gain knowledge of their own problems; some volunteered out of curiosity; on account of group acceptance; or for monetary reasons. The volunteers either were members of the hospital personnel (attendants, nurses, psychologists, doctors, research associates), or came from outside of the hospital (students, scientists). Hence a wide variety of educational backgrounds, social classes, and occupations were represented.

The method was about the same previously described (2, 36). On the "experimental day," the volunteers received LSD by mouth. Either one or one-half microgram per kilogram body weight of LSD was mixed in a glass of distilled water, and the subject drank it in the morning on a fasting stomach. In a number of cases particular controls were applied. On the "control day," which either preceded or followed an experiment, the volunteer, without his knowledge, received only plain water. As an additional control, the observers were often kept in ignorance of what the subject had received, in order to exclude a bias on the part of the observer. In one case, a more elaborate polygraphic study was made.

After the experiment had started, the volunteers were observed individually and in a group; they underwent psychological tests such as the Rorschach, Thematic Apperception, Draw-A-Person Test, proverbs, Bellevue Blocks, Concrete-Abstract Thinking, and

Drawing of Feelings. Sociological and anthropological-constitutional studies were added. About 2 hours after the beginning of the experiment, the volunteer was psychiatrically examined by DeShon. Chemical examinations pertained to the determination of the urinary excretion of 17-ketosteroids, creatinin, urinary sodium, potassium, uric acid, and phosphates. Examinations of the autonomic nervous system were done with the aid of the polygraph and pharmacodynamically, mainly on inpatients, and on a few normal volunteers. In one instance a patient who had undergone frontal lobotomy was examined before and after lobotomy.

RESULTS

CLINICAL AND SOCIOLOGICAL PSYCHIATRIC OBSERVATIONS

Our previous clinical observations on volunteers who had taken LSD were confirmed and further elaborated. In the majority of normal adult subjects, one microgram per kilogram body weight produced a syndrome simulating a moderate acute schizophrenic upheaval of the turmoil or schizo-affective type with or without catatonic features. Other manifestations were disturbances of the thought processes and of perception, behavior, affect, and mood. Misinterpretations, hallucinations, and delusional experiences were recorded when noted; suspiciousness and paranoid reactions were not uncommon. Depersonalizations were often experienced by the subject and catatonic phenomena occurred in some instances.

Hostility.—Of particular interest was the observation of hostility. Hyde, von Mering, and Morimoto (21) of our group, made this phenomenon the object of a special study on 10 subjects who had received one microgram of LSD per kilogram body weight. The focus of this study was hostility in affective interplay with other persons, and the degree and quality of distortion of these other persons that occurred under the influence of LSD. The study resulted in the observation that the strongly affective relationships of affiliative or hostile nature were distorted to a greater proportion (26%) than were relationships of impersonal, empathic, and nutritive character (6%). It appeared that

the distortions in interplay occurred primarily where the interplay was demanding or threatening. When the subject's attitude was hostile, he tended to devalue the object: "a diabolical face," "a flattened face," "a young woman looking 100 years old." When the subject's interplay attitude was affiliative, he tended to perceive the object in an overvaluing manner; for example, "big, my very rock of Gibraltar," "soft and warm, or glowing with youth and health."

These observations demonstrate that visual distortion provides more reality to the subject than his actual thoughts and feelings. These distortions cannot be explained as projection by the subject, for they were not determined by attributing his own characteristics to the interviewer. Rather, they may best be interpreted as representing an intensified awareness of his feelings toward the interviewer derived from his conception of the interviewer's attitude toward him. The sociological observer noted that subjects became hostile when treated in a cold, investigative, unsupportive, or hostile manner. The under-evaluation of the interviewer in these circumstances as shown by the distortion of his appearance seems largely the result of keener and more acute realization of interpersonal relationships by the subject under the influence of d-lysergic acid diethylamide. With such experiences we may well approach the understanding of feelings of the mentally ill.

Behavior.—Usually the behavior of a person who has taken LSD is altered. Most of the time, underactivity and loss of spontaneity are observed with a tendency to withdrawal, but occasionally overactivity occurs with aggressiveness, dramatizations, playfulness. Our sociologist, Morimoto, investigated the sociopsychological behavior of 43 normal subjects who were under the influence of LSD. An evaluation was made on each subject before he received LSD, as a basis for comparison. Each subject was classified on 35 attributes which indicated feelings and actions related to his behavior in interpersonal relationships. These attributes were further classified into 4 categories or modes which indicated in which directions one moves in interpersonal relationships. The modes of directions were: away, against, toward, and with.

The results of this intriguing study revealed that during the influence of LSD the scores in the modes, away, against, and toward, were significantly increased (x^2 significant at .001 level). A significant decrease in scores was found in the "with" mode (x^2 significant at .001 level). These observations mean that the behavior of the subject who is under the influence of LSD is altered from his pre-LSD behavior in the sense that the mode is now one of the moving *away* (avoidance, withdrawal, denial); *against* (hostile, punitive, competitive); and *toward* (seeking of nurturance, support, reassurance); while the *moving with* (brotherly, friendly, reciprocal equalitarian) type of behavior is clearly reduced. This study also indicated that the hospital personnel had more severe reactions than subjects from outside of the hospital. The ability to mobilize appropriate social behavior was reduced during LSD; the directions of change were toward greater rigidity, although a few exhibited an erratic and overreactive type of behavior (x^2 significant at $>.05 < .02$ level). Intensity of symptoms subjectively experienced increased in social situations in which there were specific expectations placed upon the subject (x^2 significant at .001). On the other hand, intensity of symptoms was reduced in those social situations that were supportive and nurturant to the subject.

One cannot escape the impression, from these observations, that the socio-psychological behavior changes showed similarities with the general behavior of the mentally ill and that they provide fundamental implications in the field of psychotherapy.

Psychological Tests.—Psychological tests reported here³ include a partial Rorschach (Cards III, VII, and VIII); Wechsler-Bellevue Block Designs (#2 and #4); Draw-a-Person Test; and 8 Thematic Apperception Cards. The interpretation of the data obtained took into due consideration such limiting experimental variables as the abbreviated testing, different examiners, test-retest effects, and differences in LSD dosage. The tests were given to 29 subjects, each of

³ The psychological examination of subjects who had received LSD was provided by our associates in psychology, Roseline Goldman, Ph.D., and Richard York, Ph.D.

whom took the tests twice; that is, with and without LSD administration. All but 2 subjects showed significant change in at least one major area of personality, such as perception, cognition, or emotion. Functioning was definitely modified in 2 or more dimensions. However, each subject clearly maintained his own way of functioning in his idiomatic style. Interesting enough, of the 2 exceptions, one was a physicist who became blind 4 days after birth; the other a subject selected because of epileptic equivalent symptoms of the temporal lobe variety which were similar if not identical to symptoms of the LSD effect.

Reduction in Organization and Integration.—The most marked change for the group as a whole was a definite reduction in organization and integration of the subjects' response to conventional features of their environment and experience. They showed a lack of concern about their behavior and responses. Their disregard for the environmental stimuli was accompanied by an increased concentration on discrete or minute aspects of experience. The subjects' attention was centered on restricted areas. There was a general loosening of critical appraisal. Intellectual control was impaired with difficulty in concentration and associative thinking.

Perceptual Distortions.—A lack of discrimination between their own feelings and those of others and an imputing of their own qualities to objects were noted. This is illustrated in Rorschach responses: One subject had originally described a red part of one blot as "two hearts beating as one." With LSD, this became "blood." The color seems to have had a stronger impact under LSD, and diminished his intellectual control. His response now seemed to be without any social implications or evidence of attempted control. Another subject who said, "that resembles genitals" responded, when under LSD, "this seems a more friendly genital now, closer to the real thing."

Loss of Emotional Control.—The loss of emotional control and the loss of control of distance between the self and the stimulus were reflected in the subjects' responses. There was reduction of delay in controlling emotional reactions to people and to the

demands of the environment, with a tendency for more individualized, unconsidered, immature reactions. In the LSD test situation subjects appeared more interested in their own feelings and inner experiences than in interacting with the examiner, confirming behaviorally the test results, which indicated increased self-centeredness.

The Thematic Apperception Test (TAT).

—Eight pairs of TAT stories were analyzed. The analysis was made in the following areas: interaction between the characters on the cards, perception of the environment, freedom in the expression of emotion or feeling. Two important features were revealed: Under LSD, roughly one-half of the subjects perceived less interaction and closeness between the characters on the cards. They viewed the environment as less warm and helping, or less interesting, and also, they were less free in expressing emotion. The other half showed no significant change from the control stories. It was often apparent that the TAT pictures became more vivid, the people in them more real. Subjects would meet this threat by devitalizing their stories or avoiding involvement.

Decrease in Orientation to Past and Future.—Associated with the decrease in interest in the environment, there was, in the stories, emphasis on the "here and now," rather than on the normal sequence of past, present, and future. Memory of past and anticipation of future involvements in personal and social events was disrupted. There was also a concentration on subjective concerns and feelings which the subjects found difficult to communicate or so intriguing as to preclude spontaneous interaction with the environment.

Wechsler-Bellevue Block Designs (#2 and #4).—On simple psychological tasks structured by the examiner for the subjects, little loss in efficiency was seen in regard to either time or accuracy in the performance. On the other hand, Hyde and other co-workers observed that volunteers of the hospital staff, who had taken LSD, had great difficulty in performing their usual tasks in the course of their routine duties.

Anxiety and Tension.—Both anxiety and tension were increased in some individuals, and decreased in others, with no consistency

for either trend in the group. Retention of basic personal identity was usually maintained in spite of the changes that occurred, presumably because the individuals were aware of the fact that the LSD experiences were temporary and possibly because of the peculiar nature of the experience which preserves insight in spite of drastic intellectual and emotional changes.

AUTONOMIC NERVOUS SYSTEM

Phenomena of the autonomic nervous system have been observed by most authors and some, Forrer and Goldner (5), Savage (37) and Hoffer (19), studied and described them in more detail. In our experiments, autonomic phenomena were observed in all instances, and always preceded the mental phenomena. They occurred as subjective feelings and were objectively confirmed by clinical observation, polygraphic recordings, and pharmacodynamic methods.

Subjective Experiences.—All subjects who had taken LSD experienced sensations which were the result of dysfunctioning of the muscular, cutaneous, gastrointestinal, genitourinary, cardiovascular, respiratory, and sensory systems. Most common were subjective feelings of trembling, while actual tremor was rarely seen, feelings of numbness, hunger, and nausea; less common were coldness and warmth, perspiration, tingling, throbbing, flushing, sighing, tightness, choking sensation, sexual excitement, and need to urinate.

Polygraphic Recordings.—Albert DiMascio, M. A., Elsie Suter, M. D., and Doris Raphael, A. B., of our research department, were predominantly concerned with the polygraphic recordings of autonomic manifestations. The experimental design was as follows: One subject volunteered for 7 experiments which were executed at 1-week intervals. At 8 o'clock in the morning, on a fasting stomach, he received a drink which was prepared by Dr. Hyde. Neither the subject, nor the observers, were informed whether the drink contained LSD or plain water, and since LSD is absolutely tasteless the subject had no way of distinguishing. A code was kept and disclosed only after all the experiments were over. It may be stated

here, however, that both observers and subject, in the course of the experiment, invariably made the right diagnosis. After the subject had taken his drink, he went through psychodynamic interviews while attached to the polygraph, and a number of physiologic manifestations were recorded, of which only the heart rate and respiration are reported here. Measurements of blood pressure and size of pupils were also made. Examinations were done at 3 periods: resting before the interview, during the interview, and after the interview. The findings are summarized for heart rate in Table 1, for stability in Table 2. As can be seen from these tables, the second, fifth, and sixth records designate LSD experiments; the first, fourth, and seventh records designate control days. The experiment on the third day has been excluded because it is not strictly comparable to the others as the volunteer had a high temperature due to incidental septicemia. The heart rate is expressed as means of the time in seconds between 2 consecutive QRS

TABLE 1

THE EFFECT OF LSD UPON THE HEART RATE
(Polygraphic Recordings)

Record No.	LSD		Record No.	Control	
	\bar{X}	SD		\bar{X}	SD
2....	.77	± .050	1....	.73	± .048
5....	.65	± .037			
6....	.59	± .044	4....	.69	± .045
			7....	.71	± .056
Average .	.67	.044		.71	.050

Rates are given in terms of seconds between two consecutive QRS complexes. The pulse rate on LSD days is higher.

\bar{X} = average.
SD = standard deviation.

TABLE 2

THE EFFECT OF LSD UPON THE STABILITY OF
HEART RATE

AVERAGE RESTING D-SCORE *

Record No.	LSD	Record No.	Control
2.....	34.58	1.....	33.42
5.....	27.74		
6.....	27.66	4.....	28.98
		7.....	34.60
Average	29.99		32.33

* D- Score—see text.
The heart rate is more stable on LSD-days.

complexes, not in pulse rates per minute. This method was chosen because pulse rates could not be handled statistically as easily and accurately as time measures. Table 1 indicates that the heart rate under the influence of LSD was higher than the heart rate on control days.

Table 2 expresses the stability of the heart rate on LSD days and control days. On analysis of the record of the automatic continuous heart beat markings, it was noted that the heart beats fluctuated considerably as to rate and degree of change. In order to quantify the rate and degree of such fluctuation, the "D-" score was devised as a statistical measure. The "D-" score is obtained by the formula $\frac{\sum \Delta d}{\sqrt{n}}$ in which Δd represents the amount of change from peak to valley measurement and n the number or recorded peak-valley changes. The change between a peak and valley must be at least .03 seconds. A large "D-" score indicates a greater lability, or in other words, instability of the heart rate. A low "D-" score indicates a relatively stable rate. Table 2 demonstrates that the heart rate was more stable on LSD days.

Respiration.—The polygraphic records reveal that LSD caused a greater variability in length and depth of the respiration cycle than was indicated on control days. Also the rate of respiration was faster, and there was more sighing.

Pupils.—Table 3 shows the size of the pupils as measured by the same observer under identical conditions. A marked change in the size of pupils occurred only on LSD days. The diameter of the pupils was 3 mm. at 9:00 a.m. on LSD and control days. However, when the subject had received LSD, the pupils, during 2 hours and 45 minutes, gradually dilated from 3 mm. to 5.25 mm. The psychodynamic interview, however, was

not influential in this phenomenon, as the controls convincingly demonstrate. They showed no appreciable change in the size of the pupils.

Blood Pressure.—The systolic and diastolic blood pressure was taken with the ordinary clinical method before and after an interview. LSD, itself, affected the blood pressure very little, although the blood pressure readings were slightly lower after LSD than on the controls. Noteworthy, however, was the phenomenon of the rise of blood pressure during LSD action following a psychodynamic interview: On LSD days the blood pressure was somewhat higher after a psychodynamic interview (average 132/94 mm/Hg). The reverse was observed on control days; the blood pressure was lower after the interview (average 125/98 mm/Hg).

PHARMACODYNAMIC EXAMINATION

The pharmacodynamic or indirect examination of the autonomic nervous system was performed with the administration of synthetic Nor-epinephrine, synthetic Epinephrine, and synthetic acetyl-betamethylcholine (Mecholyl). These chemicals were selected because of their already known relationship to emotion in general and schizophrenia in particular. Fifteen cooperative patients of the hospital, predominantly schizophrenics, were examined, with the assistance of a nurse and other observers, early in the morning, mostly on a fasting stomach. The examination took place in a quiet examining room where the patient was left to rest until the systolic blood pressure had leveled off. The patient then received an intravenous injection of one test drug; the blood pressure, and often the pulse rate, were taken and recorded at 30-second intervals for 5 minutes, and at 1-minute intervals for another 5 minutes, or until the blood pressure had returned to nearly the initial reading. This procedure was followed with the older test drugs, after a sufficient rest period between tests had elapsed. The same procedure was repeated, on the same day, 2 hours after the patient had received LSD. This procedure has since been changed because we realized that it caused too great

TABLE 3

THE EFFECT OF LSD UPON SIZE OF PUPILS
(The measurements were taken on the same person, in the same room, in the same light.)

Time	LSD	Control
9:00 A.M.	3 mm.	3 mm.
10:45 A.M. (Pre-interview) ..	4.75 mm.	2.70 mm.
11:45 A.M. (Post-interview) ..	5.25 mm.	2.75 mm.

a stress for the patient, and therefore, set aside one day for the control and, after a sufficient interval, another day for the actual LSD experiment. This change in procedure seemed fully justified, for the comparison of the effect of the test drugs on control days revealed little, or merely insignificant, variations. *Method:* Synthetic Nor-epinephrine and synthetic Epinephrine were given intravenously in the amount of 0.025 cc. of a solution of 1:1000, and acetyl-betamethylcholine (Mecholyl) was injected intramuscularly in the amount of 2.5 mg. These small amounts were given because we observed that the reactions were sufficiently distinct, and caused less discomfort. LSD was given orally, $\frac{1}{2}$ microgram per kilogram body weight, because with the usual dose of one microgram per kilogram, we encountered more severe reactions in some patients, which led to unpleasant disturbances on the ward. On the other hand, the fact was established that even $\frac{1}{2}$ microgram of LSD caused sufficient and detectable changes in the autonomic functions. Normal volunteers, however, received mostly one microgram per kilogram body weight. As an additional control, in some instances, physiological saline solutions were submitted for LSD, but the results were so drastically different from actual LSD experiments, that the saline control as a routine could be omitted.

The Effect of Nor-epinephrine.—The height of the reaction occurred within 30 to 60 seconds, and leveled off after about 4 minutes. The average rise of the systolic blood pressure during the control period was 61.5 mm/Hg, and 2 hours after the administration of LSD, it was 68.2 mm/Hg. The changes of the diastolic pressure are reflected by the pulse pressure. On the control days, the average initial pulse pressure was 47.7 mm. and the average pulse pressure at the height of the reaction 84 mm., with a difference $D=36.3$ mm. Not much difference was observed on the experimental days. Two hours after the oral administration of LSD, the average initial pulse pressure was 46.4 mm., at the height of the Nor-epinephrine reaction 87 mm., with a difference $D=40.6$ mm. A comparison of the data shows that the response of the systolic and diastolic blood pressure to the injection of

Nor-epinephrine was not much different on control and experimental days. In other words, LSD did not appreciably alter the response of the autonomic nervous system to Nor-epinephrine.

The Effect of Epinephrine.—The average rise of the systolic blood pressure, following the injection of Epinephrine, on control examinations was 85.4 mm/Hg, and 2 hours following the administration of LSD, 57.6 mm/Hg. In both instances, the height of the reaction occurred between 30 to 60 seconds. The pulse pressure was recorded as an expression of the diastolic pressure. During the controls, the average initial pulse pressure was 49 mm. and at the height of the reaction 119.5 mm/Hg, with a difference $D=70.6$ mm. Two hours after the administration of LSD, the average initial pulse pressure was 45.8 mm/Hg, and at the height of the reaction 93.3 mm/Hg, a difference $D=47.5$ mm.

The statistical evaluation of the data of the systolic blood pressures is summarized in Table 4, which indicates the mean values; standard deviation; and P-values. As can be seen, the changes in blood pressure after the injection of Nor-epinephrine are statistically not significant; following the injection of Epinephrine, the recorded changes in the blood pressure on control and experimental examinations are significant with a P-value between means of $<.01$.

The Effect of Mecholyl.—Thirteen pa-

TABLE 4

SUMMARY OF DATA

Mean Values; Standard Deviation; P-Values

	A. Nor-epinephrine			
	Mm. Hg.		D.* Mm.	
	Control	LSD	Control	LSD
Mean values	61.5	68.2	36.3	40.6
Standard deviation ..	21.4	22.4	22.4	20.6
P-value between means ..	N. S.*		N. S.	

* N. S. = not significant.

	B. Synthetic epinephrine			
	Mm. Hg.		D.* Mm.	
	Control	LSD	Control	LSD
Mean values	85.4	57.6	70.6	47.5
Standard deviation ..	14.6	10.3	19.0	15.4
P-value between means ..	$<.01$		$<.01$	

* D. is the difference between the basal and the highest pulse pressure.

tients received 2.5 mg. of Mecholyl intramuscularly. The results of this examination indicated a slightly lesser reaction of the parasympathetic system to Mecholyl after the effect of LSD had become manifested.

LSD and Lobotomy.—We had an opportunity to study both the psychological and autonomic reactions to LSD in one case of lobotomy. A female patient, aged 65, who had been hospitalized for 30 years before the lobotomy, exhibited the symptoms of an agitated depression with restlessness, fears, and anxieties. Almost immediately after lobotomy was performed, the patient had become calm, no outward signs of fears or anxiety could be detected. About 6 weeks after lobotomy, she received $\frac{1}{2}$ microgram of LSD per kilogram of body weight by mouth, and about 45 minutes later, she seemed to be back in the original state of agitated depression, expressing fears, anxieties, and feelings of guilt. This condition lasted for several hours, but subsided toward the evening.

The autonomic responses also indicated a relapse into her pre-lobotomy state. Before lobotomy, the systolic blood pressure on Epinephrine stimulation rose 70 mm. within about 1 minute, and returned to the base line after about 4 minutes. After lobotomy, as could be expected (30-34) the reaction of the systolic blood pressure to Epinephrine was greatly enhanced. It rose 110 mm. and dropped sharply within 2 minutes, without reaching completely the base line within the 10 minute time of observation, but establishing a new, somewhat higher base line of 170 mm/Hg. Following the administration of LSD, the reaction was quite different. On Epinephrine, the millimeter deviation of the systolic pressure from this new base line was a rise of about 50 mm. which, after 3 minutes, turned into a drop considerably below the base line. The effect of 2.5 mg. of Mecholyl upon the systolic blood pressure, obtained 2 hours after the administration of LSD, indicated a somewhat more pronounced reaction than is seen in nonlobotomized patients.

Summary and Discussion.—The systematic examination of the autonomic nervous system revealed that LSD seemed to influence particularly the adrenalin system. The heart

rate was higher and more stable under the influence of LSD. This recalls Witt's(45) observation of the more nearly perfect spider net built under the influence of LSD. However, the more nearly perfect webs made by spiders under LSD are at the same time much weaker, which allows the speculation that this may well be the result of an exhausted or otherwise disturbed adrenalin supply. It has been known for years that the efficiency of spider webs in clotting blood depends on their adrenalin constituent. The higher and more stable heart rate in humans under LSD may likewise be the result of changes in the adrenalin system.

The pupils became dilated from a basic 3 mm. to 5.25 mm. within 2 hours and 45 minutes, which indicates sympathetic stimulation. Similar observations on the pupils were reported by Forrer and Goldner(5) and Savage(37).

The systolic blood pressure, following psychodynamic interviews, went up on LSD days, while the reverse took place on control days. This phenomenon may be related to an increasing anxiety as the result of LSD administration.

The blood pressure response to Nor-epinephrine was not significantly altered on LSD and control days. The response to Epinephrine was lower on LSD days. In evaluating this observation, one must bear in mind that the examinations were done on mental patients whose autonomic responses are already altered by their mental condition which has been aggravated by LSD.

LSD caused only slight inhibition of the systolic blood pressure response to Mecholyl.

LSD altered the psychological as well as the physiological effect of lobotomy. One gained the impression that LSD had caused a relapse into the mental and physiological state which existed before lobotomy was performed.

ADRENOCORTICAL SYSTEM

Motivation.—The relationship of the adrenal cortex to schizophrenia which manifests itself in a reduced responsiveness of schizophrenic patients to experimental stresses and test doses of ACTH has already been established(17, 28, 29). Schizophrenic

patients excrete on the average less inorganic phosphates than normals but display a marked increase in phosphate excretion under stress or following the injection of ACTH or adrenal cortical extract, which also cause a release of endogenous corticoids. The similarity of psychological symptoms of LSD action to those of schizophrenia therefore seemed to offer an interesting investigation of adrenal cortex responses to LSD stress.

Procedure.—The following procedure was adopted: A group of normal volunteers was selected. One day was devoted to controls, another day to the actual LSD experiment. On the control day, urine was collected from the time of rising until approximately 9:00 a.m.; a second urine sample represented the urine produced from 9:00 a.m. until 3:00 p.m. At 3:00 p.m., 25 mg. of ACTH was injected intramuscularly. At 6:00 p.m., a third urine sample was collected. The urine samples were analyzed for rates of excretion of urine, creatinine, 17-ketosteroids, sodium, potassium, phosphates and uric acid. On the *experimental day*, the same procedure was followed with the exception that at 9:00 a.m., the volunteer was given orally 0.5 micrograms of LSD per kilogram body weight.

Results.⁴—The results, though still tentative, revealed interesting observations. The data as means are summarized in Tables 5 and 6.

Table 5 demonstrates the stimulating effect of ACTH on the adrenal as measured especially by the 17-ketosteroids, sodium and uric acid constituents in the control series. It shows that the 17-ketosteroid output was less by 14% in the case of the second control as might be expected from the usual diurnal rhythm. The administration of ACTH increased the 17-ketosteroid output in expected fashion. From diurnal rhythm expectation without ACTH this value in the third column would have been about 70% so that there was a rise of approximately 60% following ACTH. This table also indicates that ACTH caused a retention of sodium. There was evidence of an increased output of both sodium and potassium in the

TABLE 5
CONTROL DAY

(Mean % values per gram creatinine of 17-ketosteroids, urinary sodium, potassium, uric acid, and phosphates. Urine samples were taken at 9:00 a.m., 3:00 p.m., and 6:00 p.m.)

	1st Control	2nd Control × 100 1st Control	ACTH × 100 2nd Control	Significance
17 ks.....	100	86	128	P < 0.05
Na	100	125	83	P < 0.01
K	100	147	119	Not signif.
Uric acid.....	100	91	131	P < 0.05
Phosphates ..	100	66	162	P < 0.02

* Underlining indicates statistical significance at better than the 5% level between the 2nd and 3rd columns.

Table 5 compares the control-control-ACTH studies in terms of mean per cent changes as indicated by the column heads.

second control over that of the first; this increase was unexpected and is in contrast with the decreased output of 17-ketosteroids. The effect of ACTH on this already rather high potassium output was negligible. Uric acid showed the usual kind of response. The second control indicates the diurnal rhythm reduction over the first control; ACTH significantly enhanced the uric acid output. Phosphates also showed the kind of diurnal rhythm one would expect but there was an increased output of these phosphates with the administration of ACTH. The evaluation of these data must take into consideration that the volunteers who had no breakfast were allowed to have lunch. The midday meal may have interfered with the sequence of events, because recent findings by Elmadjian, of the Worcester group, indicates that taking of a meal produces some stress response to the adrenal. This, then, would tend to elevate signs of adrenal activity in the second control sample. The high value of potassium in the second control may limit its percentage rise after ACTH, since potassium is especially affected by the intake of food.

Table 6 shows that LSD in itself stimulated the adrenal as indicated by the 17-ketosteroid data. The 17-ketosteroids, following LSD, showed a 129% response if the first control is compared with the second control, in contrast to the reduction from

⁴ Compiled and described by Hoagland.

TABLE 6
LSD EXPERIMENT

(Mean % values per gram creatinine of 17-ketosteroids, urinary sodium, potassium, uric acid and phosphates.)

	Control	$\frac{\text{LSD}}{\text{Control}} \times 100$	$\frac{\text{ACTH}}{\text{LSD}} \times 100$	Significance
17 ks.....	100	<u>129</u>	<u>113</u>	P < 0.05
Na	100	<u>136</u>	<u>89</u>	P < 0.05
K	100	<u>113</u>	<u>131</u>	Not signif.
Uric acid.....	100	<u>196</u>	<u>107</u>	Not signif.
Phosphates ..	100	<u>29</u>	<u>280</u>	P < 0.05

* Underscore indicates statistical significance at better than the 5% level between the 2nd and 3rd columns.

In this table the control and LSD samples are compared, and the effects of ACTH following the effects of LSD are tabulated.

100% to 86% in Table 5. The output of sodium was increased, following LSD, but little change was seen in the potassium output. The output of uric acid was decidedly enhanced, an indication of the probable release of corticoids. On the other hand, the output of phosphates was markedly reduced following LSD stimulation. This is of interest in view of the observation that schizophrenic patients at rest excrete, on the average, only about one-half the urinary phosphates produced by normal controls (17). The absolute values of phosphate excretion are particularly illuminating. The subjects excreted 0.291 mg/gr creatinine of phosphates between 9:00 a.m. and 3:00 p.m. on the control day and only 0.162 mg/gr creatinine ($P < 0.05$) for the same period on the experimental day, under the influence of LSD, which represents a ratio of 1.8 to 1.0. This ratio of 1.8 is similar to that of 2.1 which results when the ratios of normal to schizophrenic phosphate excretion at rest is compared (17). LSD further caused a damping effect upon ACTH stimulation as can be seen in the response of the 17-ketosteroids, sodium and uric acid, in the third column of the table.

Of more interest was the observation of a marked increase in output of urinary phosphate when ACTH stimulation was preceded by the oral LSD administration. The schizophrenic patient, at rest, excretes comparatively little urinary phosphate, but the output of urinary phosphate is very large

in schizophrenics compared with normal controls following stress and after the injection of adrenal cortical extract or ACTH (17, 29). Table 6 also shows that LSD depresses the urinary phosphate output, but, once the subject was under the influence of LSD, the injection of ACTH markedly increased the output of urinary phosphate. This indicates a striking parallel between subjects under the influence of LSD and schizophrenic patients whose resting output of urinary phosphate is low, while their response to ACTH injection is greatly increased.

Summary.—LSD appears to stimulate the pituitary-adrenal axis, probably after the manner of a nonspecific stressor. It seems to render the adrenal somewhat unresponsive to ACTH stimulation, as schizophrenia causes the adrenal to be subnormally responsive to ACTH; a comparison which is quite suggestive. These statements apply to the urinary constituents which were measured and not to eosinophile, lymphocyte, or corticoid changes which were not measured (17). LSD depresses the urinary phosphate output but markedly increases it under the additional stimulation of ACTH. This behavior of the inorganic phosphate follows the pattern that was found in schizophrenic patients.

Discussion. The question presents itself as to whether the damping effect of LSD upon ACTH is specific for LSD. It could be that any injected nonspecific stressing agent would leave the adrenal refractory for a few hours so that it would be somewhat unresponsive to ACTH. No conclusive answer to this question is yet available although some degree of specificity resides in the peculiar behavior of the urinary inorganic phosphates which so closely resembles the behavior of these phosphates in schizophrenics, both as to their repression by LSD and their over-response to ACTH when the subject is under the influence of LSD. More experiments are needed before too much weight can be attached to any of the observations which are here recorded.

REFLECTIONS ON A CHEMICAL THEORY OF PSYCHOSIS

The diethylamide of d-lysergic acid (LSD), a partially synthesized derivative

of the ergot alkaloids, produced an experimental psychosis, or, to use R. Fischer's (3, 4) terminology, "model psychosis." Its mental, physiological and chemical phenomena resembled those of natural psychotic states. Other chemicals, especially mescaline (1, 14, 18, 20, 27), produce similar mental conditions. Therefore, one cannot assume a specificity of either LSD or mescaline in the causation of psychotic syndromes. The possibility suggests itself that either chemical may act by interference with an enzyme system of the organism. Such interference may originate metabolites which could be the cause of psychotic manifestations.

Glucose is the chief substrate of the brain; it supplies most of the energy required to maintain cerebral function. Mayer-Gross, McAdam, and Walker (25, 26) investigated the influence of LSD upon the carbohydrate-metabolism. They found that LSD partially blocked the carbohydrate-metabolism at the hexosemonophosphate level. However, they were unable to correlate satisfactorily the intensity and duration of the LSD-induced mental phenomena with the changes in the blood chemistry. An attempt to counteract LSD-symptoms by raising the blood level of glucose to 200-300 mg/100 ml. had only little effect and was of short duration (3-5 minutes). Our own attempts to prevent or neutralize LSD manifestations by injecting glucose to raise the blood glucose level to 200-300 mg/100 ml. were unsuccessful.

Our thoughts were early directed toward the possibility of the involvement of the adrenalin system. We noticed that symptoms of a disturbed autonomic, particularly adrenergic, system always preceded the occurrence of mental symptoms, an observation which has been reported by almost all investigators. Of special interest were such psychological phenomena as hostility and anxiety. Cannon, Funkenstein (6-12), of our hospital, Goodall (13) and others, had already published experimental observations which demonstrated the relationship of Nor-adrenalin and adrenalin to such emotional manifestations. Liddell and Weil-Malherbe (23) determined the effect of LSD upon the plasma adrenalin concentration. They reported that following intravenous LSD ad-

ministration, 3 phases could be distinguished: an initial rise of the adrenalin level, a drop below the starting level, and finally a secondary rise. In correlating the clinical and biochemical events, they observed that the phase of falling adrenalin concentration seemed to be associated with relaxation and euphoria; the rising adrenalin concentration, on the other hand, with tension and anxiety, often accompanied by a sensation of shivering and appearance of gooseflesh.

The possibility of an involvement of the adrenalin cycle in mental conditions did not seem surprising in the light of the fact that a number of clinical conditions are related to the Phenylalanine-adrenalin cycle. Martin (24), in his most informative book on Biological Antagonism, reminds us of the following clinical entities which indicate inborn errors of the phenylalanine-tyrosine metabolism: albinism, which is characterized by abnormal deficiency in the formation of melanin, a defect which is probably due to the absence of an enzyme capable of converting dihydroxyphenylalanine, an intermediary compound of the adrenalin cycle to melanin. Another condition is alcaptonuria, characterized by the excretion of homogentisic acid which, especially with alkali, turns the urine black. The phenylpyruvic acid oligophrenia has more recently become generally known. The metabolic abnormality of this condition is localized at the point of oxidation of phenylalanine to the p-hydroxy compound. Tyrosinosis, the urinary excretion of Tyrosin, is characterized by blockage at the next point of Tyrosin metabolism, namely p-hydroxyphenylpyruvic acid. Premature infants excrete p-hydroxyphenylpyruvic acid and p-hydroxyphenyllactic acid in the urine, an abnormal state which is associated with and corrected by ascorbic acid. Martin (24) points out that these clinical entities represent "metabolically mutated biochemical states," some of which "may be due to specific naturally occurring metabolic analogues."

Osmond and Smythies (27) published in 1952 an imaginative essay on a "New Approach to Schizophrenia," in which they expressed the possibility of the involvement of the adrenalin-cycle in the origination of mental illness. They were studying the

mental effects of mescaline and became aware of the structural similarity of the mescaline molecule with the adrenalin molecule. They postulated the presence of a substance M (apparently derived from the word Mescaline), which they thought originates in the organism and causes mental changes in predisposed people. In a subsequent paper, Hoffer, Osmond, and Smythies (20) further elaborated on this possibility. In their search for the substance M, they came upon adrenochrome, a metabolite of the adrenalin-cycle, which they thought most promising for further investigation. Hutcheon of their research group synthesized adrenochrome and all their further "studies were made with this synthetic adrenochrome." The authors performed 7 or 8 experiments. Adrenochrome was given subcutaneously in the amount of 0.1 mg. to 5 mg. and intravenously 10 mg. were given. The main psychological features of these experiments were reported as overactivity, poor judgment, lack of insight, depression, and hallucinatory experiences. Two dramatic descriptions of self-experiments on the same subjects are offered as further illustration. The reports indicated that the subjects had, indeed, most interesting experiences of a psychotic nature, and it is only natural that the authors arrived at the conclusion that "adrenochrome has psychological properties similar to those of mescaline and lysergic acid."

In view of the importance of these findings, and stimulated by their attractive descriptions, we tried to duplicate the experiments of Hoffer *et al.* (20). We obtained adrenochrome, which is commercially produced in this country and, for its hemostatic effect, widely used in surgery. The commercial adrenochrome was purified by linking it to Semicarbazid, one of the usual chemical reagents, and a crystalline product, adrenochrome monosemicarbazone was obtained. The addition of sodium salicylate made the crystals easily soluble in water. Each of 5 normal subjects received, orally, 5 mg. of adrenochrome semicarbazone in the early morning hours, and then was observed for the rest of the day at the hospital. The oral administration was chosen because the injection is painful, and no difference in effect was reported between the oral and intra-

venous use of the chemical. No unusual mental phenomena were observed to occur, and no subjective or objective signs of a disturbed nervous system were noted. The subjects went about their daily routine as usual. Sherber (38), who published a paper on the use of adrenochrome in surgery, in a personal communication advised us that he had never noticed any mental reaction from this adrenochrome in the more than 100 patients who had taken it.

The difference in the results of our adrenochrome experiments and those reported by Hoffer and his group may be due to the difference of the molecular structure or the stability of the product. The adrenochrome that was synthesized by Hutcheon was described as "unstable" and "deteriorating." This may indicate that other toxic substances had formed in the solution that was used by Hoffer and his group. We do not know what these substances were, but it has been reported that a further oxidation product of adrenochrome is adrenoxine.

Adrenoxine, the molecular formula of which is not yet known, was first described by P. Heirman (15, 16). In his report on "*l'adrenoxine, adrénaline oxydée inhibitrice*", he stated that the oxidation of adrenalin and tyramine by tyrosinase forms adrenochrome, but if the oxidation by tyrosinase is continued, a new substance is formed which inhibits the inotropism and chronotropism of the frog's heart. He gave this new substance the name "adrenoxine." The physical and chemical properties of the solution of adrenoxine were described as follows: The solution is slightly pink and stable for 4 days, if kept on ice. On evaporation, a residue is obtained which is slightly yellow if dissolved in water. Adrenoxine is stable in boiling water for 15-20 minutes. It is soluble in distilled water, ethyl alcohol, methyl alcohol, slightly soluble in chloroform and insoluble in ether. Higher temperatures of distillation at 100° C. accelerate oxidation and melanine appears. Physiologically, the effects of adrenoxine are characterized by bradycardia, slight fall in blood pressure which may last from 1½ to 2 hours. On autopsy, ventricular fibrillation, vasodilatation of the vena cava inferior and mesenteric veins were noted.

The authors did their experiments on animals.

The similarities of the physiological effects of adrenoxine, LSD, and mescaline may seem to warrant the study of the effect of adrenoxine on man. Adrenoxine, of which the constitutional formula has not been established as yet, may well be the adrenalin metabolite which may further advance our knowledge of the chemical relationship to the origination of psychosis.

Many data have been accumulated which allow thinking in chemical terms in relation to mental disorders. One could speculate that at one time or another in the life of a human being an enzymic disturbance in the synthesis or decomposition of a vital chemical may occur and a metabolite may originate which, in turn, causes the psychosis with its associated physiochemical changes. Which chemical actually is involved, we do not yet know, but recent research tends to indicate that the adrenalin cycle *may* be involved. Whether psychological distress affects the adrenal cycle, as Hoagland's work (and others) seems to indicate, or whether congenital factors are involved, one cannot answer as yet. What form of psychosis would result from such metabolic chemical change may depend on the age and constitution of the individual. A brief survey, on 27 male subjects, of the relationship of somatotype to the emotional or psychiatric manifestations of LSD-induced experimental psychosis was done by Philip Slater, M. A., sociologist of our group. In classifying the subjects, a method was used that was developed by the physical anthropologist, E. Hooton, of Harvard University, not the technique described by Sheldon *et al.* The findings seemed to indicate that ectomorphs tended to be intrapunitive, and mesoendomorphs extrapunitive (x^2 significant at .01 level); and clinical psychiatric classification showed a slight trend for the endomesomorphs to be affective, while the ectomorphs tended to be withdrawn.

The evidence currently available indicates that the adrenal cycle may play an important part in the development of psychoses and points up the necessity of relating the various observations in a consistent theory to further more constructive research in the field. Such

well-grounded theoretical hypotheses make explicit the need of further careful experimentation, and may furnish a substantial basis for the development of experimental psychiatry.

SUMMARY

1. Experimental psychiatry, *i.e.*, the comprehensive study of experimentally produced psychosis, is important for the advancement of psychiatry.

2. The diethylamide of d-lysergic acid (LSD) has proven an excellent tool for investigation of experimentally produced psychotic-like manifestations.

3. Clinical, psychological, physiological, and biochemical evidence is offered which indicates that the adrenalin system is involved in the LSD-produced emotional and psychotic phenomena.

4. Theoretical reflections concerning the enzymatic adrenalin system as the basis of the development of schizophrenia and other psychoses are reported.

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DISCUSSION

HERMAN C. B. DENBER, M.D., (Ward's Island, N. Y.)—It is a pleasure to discuss this well-conceived and admirably-planned venture into the new frontiers of psychiatry—the fields of experimental and pharmacodynamic psychiatry. The availability of substances capable of producing clinical syndromes analogous to the major psychoses now makes it possible to study these entities in the laboratory. The delineation of the experimental findings is precise and concise. No addition can be offered nor can any subtractions be suggested. I will address myself more particularly to the theoretical formulations that Drs. Rinkel, Hyde, and Solomon have made on the basis of their data. It is not surprising that they found in a patient following lobotomy that "LSD had caused a relapse of her mental and physiologic state." Paul H. Hoch has shown in some 50 cases that mescaline reactivates the psychotic symptoms in patients following psychosurgery. My collaborators and I have been able to show that the same takes place following electroconvulsive therapy.

While great emphasis has been placed upon the symptoms of autonomic nervous system dysfunction, it is a fact, as has been shown in this paper, that

these are merely the anlage of the mental changes that follow. They can be considered as the initial reaction to any stress-producing stimulus. In the case of LSD or mescaline, they appear almost immediately following the injection of the drug and soon give way to the acute picture so well described herein.

Rinkel and his collaborators have developed very carefully the clinical, psychological, physiological, and biochemical evidence to support their concept that the "adrenal system" is involved in the LSD produced psychosis. This is based in part upon the findings by Osmond and Smythies that the chemical structures of mescaline and adrenalin are very closely related. Rinkel states, however, that mescaline and LSD are very different not only in chemical structure but in potency as well. The fact that other drugs with even more striking differences in chemical formulae can produce disorders of the mood and thought, suggests strongly that the final clinical picture does not result from interference with a peripheral metabolic function but is probably centrally dictated. While it is undoubtedly true that the adrenal cortex alone or in combination with other endocrine glands plays a role in the production of abnormal behavior, the question still arises whether or not this is primary or secondary.

If a disorder of the adrenalin cycle is causative, how can we explain the fact that the intravenous injection of mescaline in epileptic patients not only suppresses completely spike-wave patterns and high voltage slow wave bursts which originate in the diencephalon, but also produces lethargy, drowsiness, or sleep as the major clinical reactions. These are directly contrary to those symptoms elicited with either LSD or mescaline in schizophrenic patients. In only 1 of 12 epileptic patients was it possible to produce an acute psychosis, and this patient was shown subsequently to suffer not only from epilepsy but from schizophrenia as well.

If it is a defect in the adrenalin cycle that plays such a role in the production of a psychosis, treatment then could be directed at the adrenal medulla by either denervation, or curettage, or electrolytic

destruction. Man can subsist without the adrenal medulla and with only one-fifth of the cortex. Recent reports of bilateral adrenalectomy in the treatment of schizophrenia have not led to any widespread adoption of this therapy.

I quite agree with Rinkel that a cellular enzymatic disturbance is probably at the root of many mental disorders. Freud, in his earlier papers, already speculated on the possible chemical etiology of the neuroses. However, there is far more substantiated evidence rather than mere speculation to show that the metabolic disorders at the cellular level exist not in the glands but in the central nervous system.

In terms of the cycles through which we pass, the present decade can be called the adrenal era. Other similar eras have come and gone. At one time the gonad was implicated. If we think of the body in terms of an integrated whole, it would be seen that dysfunction, as in the psychosis, represents a complex interaction of many organs. Perhaps "the adrenal cycle" is involved, but there are many other deranged metabolic processes as well, not only in the adrenal gland but in the other glands and in the central nervous system. Kallman has shown how the genetic processes are involved in mental illness. The role of psychologic factors and environmental influences have been well documented. If we study all of these derangements as a totality, I feel that a truer approach to mental disorders will be possible.

It must be borne in mind that afferent stimuli, either visual (light waves), or auditory (sound waves), can produce dramatic alterations in the set of the individual. What are the pathways of these stimuli? How do light waves and sound waves affect cellular metabolic processes? These are basic questions which still remain to be answered.

These comments are not intended to detract from the excellence of this work. Where others have simply knocked at the door, Rinkel and his co-workers have pushed it ajar. Beyond lies the answer to the most intriguing question in psychiatry today—the etiology of schizophrenia.

STUDIES OF THE PROCESSES OF AGING. X: THE STRENGTHS AND WEAKNESSES OF PSYCHIC FUNCTIONING IN THE AGED^{1, 2}

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INTRODUCTION

The complexity of the problem created by our aging population is demonstrated by the material accumulated during the First National Conference on Aging and thereafter published as a book, entitled *Man and His Years*(1). In order to develop methods of solving the problem of our elderly persons, it is important for us to know what strengths and weaknesses of psychic functioning are most likely to be present in the aged so that we can avoid complications and exploit assets to their utmost extent. In reviewing the literature, our impression is that many of the statements are based upon anecdotes and are biased. That our knowledge is insufficient was clearly recognized by the participants of the First National Conference on Aging, and a repetitive thought is expressed in almost every chapter to the effect that "Research in this area is required" or "Needed research should first be undertaken."

METHODOLOGY

This investigation, utilizing a multi-disciplinary approach, was initiated a few years ago to study some of the psychological and physiological changes which appear in old age and to evaluate their interrelationships and their effects upon the central nervous system. The number of subjects we have studied to date exceeds 332. These subjects were separated into various groups which were determined by social and economic status and medical conditions. Sixty years of

age was arbitrarily established as the lower age limit for our subjects, and no upper-age limit was set. Routine work-ups for each subject included the following: (1) detailed social and medical histories, (2) blood and urine studies, determination of NPN and fasting blood sugar, (3) physical and neurological examinations, (4) psychiatric evaluation, (5) electroencephalogram, (6) termination of critical flicker-fusion frequency for light, (7) psychological testing, which included a Rorschach, a shortened form of the Wechsler-Bellevue, the Weigl color-form sorting test, and the successive eights test.

As previously mentioned, the subjects were divided into various groups, utilizing specific criteria. For the purpose of this presentation, we shall limit our discussion to those groups referred to as "community groups" and one hospitalized group. All the elderly persons in the community group were considered to be making an adequate social adjustment and were initially believed to be free of any disease which directly involved the central nervous system. Any disease recognized prior to the inclusion of a subject in our study was considered to be minimal for the subject's age. Those placed in the community group *A* were unemployed, considered to be indigent or semi-indigent, and were recruited as volunteers from the facilities of a university clinic. This group includes 100 subjects—52 women and 48 men. The average age is 70.9 years.

Community group *B* was made up of persons who were retired, but making a satisfactory adjustment in the community. They were all of higher financial status than those placed in group *A*. The number of persons in the community *B* group was 50. However, all the data presented are not necessarily based on this complete series. The smallest number of subjects in the community *B* group, utilized for statistical purposes, was 30. The average age was 72 years.

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² This investigation was supported by a research grant from the National Institute of Mental Health, of the National Institutes of Health, Public Health Service.

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The C group was the smallest and included 40 subjects, all of whom were working, although past the usual age of retirement. Their average age was slightly less than 72 years. A small community D subgroup will be briefly referred to, composed of 10 physicians, with an average age of 75 years. All of them to various extents were continuing their interests and activities in medicine.

The hospitalized senile group was made up of 100 persons, who were admitted to a psychiatric unit because of what was believed to be either senile or arterio-sclerotic brain changes. The average age in this series was approximately 77 years.

REVIEW OF PREVIOUSLY REPORTED FINDINGS

From time to time we have reported some of our findings regarding elderly persons. Some of the accomplishments which we consider significant are felt to be worthy of review and will be referred to when we consider new data and make certain correlations. Our original observation(2) of the electroencephalographic changes in elderly persons has not altered as our number of subjects has increased. We reported a high percentage of focal dysrhythmias, which were found primarily in the left temporal areas. The presence of this focal dysrhythmia alone does not seem to impair functioning, as measured by psychological testing and psychiatric evaluation. However, if the subject had a diffuse dysrhythmia, it was usually accompanied by evidence of intellectual deterioration. In spite of the high incidence of left-temporal disturbances, we have been unable to find any correlation between handedness, cerebral dominance, or generalized vascular changes. Psychological testing indicates that persons with diffuse dysrhythmias have a decreased facility to communicate, as well as lower clarity of perception; concreteness increases in concept formation; psychomotor speed is greatly reduced. As would be expected, a significantly high percentage of diffuse disturbances was found in the hospitalized group, and the expected psychological changes were present. Subjects who continue to work after the usual age of retirement have a higher intellectual capacity than those who do not, and the electroencephalograph indicates that, physiologically, their

brains are functioning in a manner which more closely resembles records of younger individuals(3).

We have also explored some of the areas of current adjustment. It was found that elderly persons who had poor relationships with their children could be correlated with a life-long pattern of neurotic and immature behavior. Evidence collected by us indicates that religious feelings do not increase in elderly people and that there is a shift to a less strict adherence to religious dogmas. Sexual adjustment in early life strongly influences the presence or absence of sexual drives in the declining years. Individuals who had made a poor sexual adjustment in early life had a high likelihood of being free of sexual feelings in advanced years, and erotic drives disappear earlier(4).

RECURRENT PERIODS OF DEPRESSION

The problem of depressive periods in normal old people is a serious one. Karl Stern and co-workers have reported their observations, and we are in accord with a number of their findings. Mood changes and actual periods of depression occur in the lives of younger adults. However, a significant portion of our subjects reported a definite increase in frequency and depth of depressive episodes. During such episodes, the subjects reported that they felt "discouraged," "worried," "troubled," etc., to a degree that they would often feel that there was no reason to live. Frequently they wished that a painless death would intervene and a few entertained suicidal thoughts. Only one subject in the community A group revealed a suicidal attempt. The depressive periods that we considered statistically occurred at least once a month, and their duration varied from a portion of an hour to a few days. The subjects reported that these episodes of depression had not occurred in their younger years. They were often aware of the precipitating factor—usually a specific event which would initiate a chain of thoughts. Therefore, these episodes can be termed "reactive" depressions. In the various community groups, series A revealed the highest percentage, with 48% experiencing such depressive episodes. This was closely followed by com-

munity *B* group with 44%. The frequency dropped to 25% in the series of elderly individuals who were continuing to work. Although this would make it appear that working alone plays some vital role in preventing or decreasing the number of depressive episodes, it is possible that there is an underlying difference between those persons in the various groups, which permits some persons to continue to work, as well as to decrease the number of depressions.

We, in a previous report, mentioned our observation that guilt was comparatively an unimportant dynamic force in the psychic functioning of "normal" elderly persons. We do not feel that the essential mechanism in these depressive episodes is the turning inward of an unconscious, hostile impulse, which is unacceptable to the ego. The loss of self-esteem is not the result of wrongdoing, but is the result of a recognition of weakness and an inability to obtain necessary narcissistic supplies or to defend against threats to security. As previously mentioned, approximately 85% of the subjects in the community group were able to trace the onset of depressive periods to some specific stimulus. The stimuli were usually related to a suggestion that the subjects might be forced to experience increased physical suffering or lowered financial, professional, or social status. Entwined in these depressive episodes is the change which is forced upon them, regarding body image. Elderly persons are consciously aware of the inability of their bodies to readily and defensively respond to stress.

We do not believe that the fundamental mechanisms in these depressions are the same as those encountered in psychiatric practice dealing with either neurotic or psychotic depressions. The depressions do not appear to be attempts on the part of the subject to force an object to give necessary supplies nor do they appear to be regulatory attempts aimed at placating the super-ego. The possibility that both physiological and unconscious influences contributed to the onset and extent of the depressive periods must be considered, and possible interrelationships will be presented.

WORK, PLANNED CREATIVE AND RECREATIONAL ACTIVITY

Work, planned creative and recreational activities are important to elderly persons. To determine a satisfactory level of planned activity is very difficult, as it can be viewed from several standpoints, including the degree of satisfaction gained by the individual and the actual number of hours consumed. In this evaluation we used a rather complicated system which, admittedly, is not entirely satisfactory, in an attempt to determine the amount of time each subject expended participating in planned, creative and recreational activities and work. By work, we meant some endeavor which was entered into for financial gain. All subjects in community groups *C* and *D*, therefore, received considerable credit for their work activities. If an individual had less than 4 hours of his day occupied by planned activities, we arbitrarily considered this person in the "doubtful" category. Consequently, the employed group would automatically qualify as satisfactorily fulfilling the allotted amount of time. However, when we closely inspected these elderly employed individuals, we found that 60% had many interests outside of their work, which occupied a good portion of their spare time during weekends, holidays, and evenings. No one of this group was without resources of this type. When we inspected the amount of time put in planned activities by group *A*, we found that only 20% reached a satisfactory level. Sixty-seven per cent were considered doubtful, participating in a varied amount of planned activity, while 13% seemed to have nothing whatsoever to do to occupy their time, other than perhaps keeping appointments with physicians and other service persons or agencies. The community *B* group fared slightly better in that 24% appeared to occupy time in a satisfactory manner. Sixty-three per cent were occupied to some extent, while 10% were devoid of purposeful activities.

The evaluation of such activities prior to hospitalization in the senile *A* group was not considered satisfactory by the investigators. At times the knowledge of the individuals questioned was inadequate, and the reliabil-

ity of the information obtained is definitely colored by the prejudice of the informant. For instance, it is not unusual for informants to try to find some excuse for the patient's inability to maintain a satisfactory relationship with his family and community. The informant is apt to seize upon an explanation, such as follows:

He hasn't done anything to keep himself busy for the last 5 years. He always expected us to provide entertainment for him. If he had tried, he would not have gotten into difficulty as he is now.

With these reservations in mind, we would like to set forth our findings. Fewer than 3% of the hospitalized group kept themselves reasonably occupied with planned activities some time during the year prior to their hospitalization. Of course, it is probable that organic changes are related to this very small percentage of persons capable of participating in this type of effort and for this reason, it seemed wise to attempt to determine their activities several years prior to hospitalization. When this was done, we found that 57% of the hospitalized group had no reported planned recreational or creative activities.

The type of time-consuming, planned activity engaged in by various community groups, was investigated and tabulated. The various categories included: activities concerned with the family, church, social or political organizations; professional study, intellectual pursuits not related to previous professional work, physical activity, mechanical endeavors requiring the use of hands (handicrafts), artistic pursuits, and collecting. We also considered pastimes thought of as predominantly "receiving." By this, we mean a planned activity which requires little or no participation by the subject—merely his attention and his effort to get to the spot where the "receiving" was to be done. In this group we considered radio and watching television, motion pictures, dramatics, etc. The vast majority of all of the subjects was in the habit of listening to the morning weather report and to news broadcasts. A few isolated radio programs were often selected to listen to during the week, but relatively little time was occupied in this way. It should be noted that television

had not gained a firm foothold in the area in which these subjects were examined, and it is possible that within a relatively short time a much greater number of elderly persons will consume their leisure hours by watching television. However, the habitual use of such receiving activities was found to be much higher in the indigent or semi-indigent group than in any group of higher financial status. Intellectual activities were stable reaching approximately 30% in all groups. If it is possible to utilize as a rough measurement the apparent enthusiastic response of the various subjects when discussing their recreational activities, it appears that most satisfaction is derived from those hobbies which are creative or that add to the satisfaction gained from the intellectual achievement. It is our impression that these persons who have no planned activity or those who devote time to "receiving" activities are much more prone to depressive episodes than those who, through their own efforts can receive satisfaction.

The ability to participate in creative activities is very much influenced by the extent of the education of the subject. Education is important in developing diversified interests and abilities, which are particularly useful as resources in old age.

CONSTIPATION

The frequency of constipation and the habitual use of laxatives is often referred to as the most common problem which confronts the physician who is treating elderly patients. We considered our subjects habitual users of cathartics if such medication was employed once a week or more. Twenty-seven per cent of community *A* group were chronically constipated; 20% of *B* group and 16% of *C* group. From these statistics, it is reasonable to conclude that approximately 25% of elderly persons require laxatives at least 2-4 times a week. Fifty per cent of all the subjects used laxatives either habitually or occasionally. Those subjects who occasionally required a bowel stimulus were frequently aware of a connection in a specific emotional disturbance and the onset of constipation. In the women subjects the dis-

turbance was usually related to some difference of opinion which developed between the subject and a daughter-in-law or son-in-law.

No consistent, specific personality features were detected in the subjects who were chronically constipated. A few showed traits similar to those usually encountered in young adults who manifested bowel disturbances as a neurotic symptom. It is, therefore, our feeling that chronic constipation in elderly persons is related to organic changes in a high percentage of cases.

INSOMNIA AND SEDATION

Nocturnal sedation—the use of sleeping pills—was employed by 30% of *A* group, 25% of *B* group, 20% of *C* group, and 40% of the physicians studied. None of the physicians was an habitual user, yet it is quite possible that free access to such medication was responsible for the higher incidence but the size of the group and higher average age must be considered. Seven per cent to 10% of the community groups were habitual users of sleeping pills. All these individuals had numerous other problems which presented evidence of a poor adjustment.

CORRELATIONS AND CONCLUSIONS

Correlations utilizing the incidence of depressive episodes as the constant were made with other data.

We were unable to correlate depressive episodes with the physiological changes of the brain as measured by the electroencephalograph. Since our subjects were selected as in relatively good health, the attempt to correlate physical condition and depression was unrewarding. Equally unrewarding was the possible exploration of the role of marital status and housing facilities. Chronic constipation was not significantly higher in the depressive subjects.

We previously mentioned the high incidence of consciously recognized, specific events believed to be the precipitating factor in depressive episodes. Defenses against periods of depression were apparent. Those individuals who were relatively free of depression had certain patterns of behavior and psychic functioning which they utilized as a means of attaining satisfactory adjust-

ments. Those subjects who continued to occupy their time by working had an excellent method of warding off such episodes; those subjects who engaged in adequately planned creative activities fared equally well. These same subjects were very apt to participate in social, political, or professional groups, but again it was evident that this was no new pattern of behavior and that these individuals had participated in groups for many years. Although such defenses seem to be the most adequate, they do not guarantee that the subject will not suffer depressive episodes, for there were isolated individuals who reportedly used defences as good as those previously mentioned, yet were the victims of periods of depression.

Verbalized excessive hypochondriasis was invariably linked with depressive episodes, and feelings of neglect and persecution were found in close to 60%. Nearly all of these persons with verbalized hypochondriasis had a poor relationship with their children. This may be interpreted as the result and not the cause. Fortunately, in a previous study we had rated the subjects as to their parental role in younger years. Eighty per cent of this excessively hypochondriacal group were parents who had been rated as poor mothers and fathers.

Evidence acquired from psychological testing indicates that many elderly persons have little capacity to express warm and spontaneous feelings toward others. The cause of this is undoubtedly complex, but it appears that elderly persons are, in a sense, "misers" of their affections. They are fearful that if they invest an object with positive feelings, it is unlikely that such feelings would be returned, and for this reason they feel that their efforts would be fruitless.

We have reviewed some of the numerous influences that affect the psychic functioning of elderly persons. We believe that adequacy of adjustment in the elderly is largely determined by strengths and weaknesses developed much earlier in life. Although we agree that elderly persons deserve the attention of our society, we believe that it would be more advantageous to devote time and effort to ways of preparing people for old age and to concern ourselves with preventive techniques.

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THE PATHOLOGY OF SENILITY¹

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The word pathology is defined as the science of the origin, nature, and course of diseases, also the sum of morbid conditions and processes in a disease. If old age and senility were considered synonymous, then to describe the pathology of senility it would be necessary to start before birth. As Henry Vaughn wrote years ago:

Though we dye but once, yet do not dye at once. We may make, yea we do make many assaies or tryals of dying: death insinuates itself and seizeth upon us by peacemeals—so soon as we begin to be, we begin to wast and vanish, we cannot ascend to life without descending toward death: Nay, we begin to dye before we appear to live, the perfect shape of the infant is the death of the embryo, childhood is death of infancie, youth of childhood, manhood of youth, and old age of manhood.

However, it is also true that a life may seem long because it is boresome and may be too short because one has so much to do. A long life, in other words, does not depend entirely on the number of years lived; longevity is not necessarily a cause for senility, nor is old age an excuse for helplessness.

According to Shock(1) the problems of gerontology fall into 4 main categories: (1) the general biology and physiology of aging; (2) the psychological changes with age; (3) pathological deviations and disease processes; (4) the socio-economic problems of an aging population. The pathology of senility, the subject of this paper, should be a discussion of those factors in each of these categories that tend to turn normal senescence into senility. Senility, according to the dictionary(2), indicates a state of being old, but modern usage, especially psychiatric custom, has changed the meaning of the word to indicate a pathological state definitely separate from normal aging.

Noyes, in the recent edition of his text(3), describes in splendid fashion the change of normal old age into senility. This change is often a gradual one. The day-by-day alterations may be so slight that they are imper-

ceptible, or the changes may be episodic and so outstanding that it is obvious that death has taken another bite.

A dislike in change, a reduction in ambition and activity, a tendency to become constricted and self-centered in interests, an increased difficulty in comprehension, an increase in time and effort necessary for the performance of familiar duties, an increasing difficulty in adapting to new circumstances, a lessened sympathy for new ideas and views, and a tendency to reminiscence and repetition are scarcely signs of senile dementia, yet they pass imperceptibly into mental destitution and personality regression[3].

It is the thesis of many gerontologists that this process starting with the dislike of change and ending in mental destitution and personality regression is not necessarily a part of the aging process and that by studying the problems of aging such destitution and regression can be prevented.

In 1945 a Division of Adult Hygiene and Geriatrics was established by the Indiana State Board of Health. This division, under the leadership of Dr. William F. King, has 5 definite objectives. The first 2 are: (1) to study the factors of life that are related to senescence and senility as these are influenced by age, environment, heredity, and the diseases and disabilities associated with advancing years; (2) to help the public know that senescence is normal, that senility is not a necessary part of age, and that through better understanding and cooperation much of the premature deterioration of aging can be prevented(4). The process of becoming senile is the process described above. It starts with an increased constriction of activities and ends in mental destitution, and the pathology of senility is concerned with study of the characteristics of this change, from normal senescence into mental decay.

The aging process has become a popular subject for study and for discussion during the last 10 years. Panel discussions, lecture series, and many journals are devoted to the subject of geriatrics or gerontology. Therefore it is very difficult at this late date to present data that have not been presented before. Nevertheless, the problem here

¹ Read at the 110th annual meeting of The American Psychiatric Association, St. Louis, Mo., May 3-7, 1954.

offered, namely, why people become senile, is still new because, although studied and discussed over and over, this problem still remains one about which very little is known.

In this presentation of recent data regarding the pathology of senility, it was thought best to follow the approach of Shock, mentioned above: first to discuss the ideas concerning the general biology and physiology of the senile process and follow this with a presentation of pertinent findings reported in the recent literature, then discuss in similar fashion the psychiatric and psychological characteristics and recent findings, and finally the socio-economic factors that seem to affect the senile change.

In the field of biology and physiology, which would include eugenics, anatomy, and biochemistry, it has been felt that the personality changes known as senile are a definite function of the cells of the cerebral cortex. The factors that cause cell change might involve the enzyme systems, the intracellular, extracellular fluid balance, the cerebral blood flow, and cerebral metabolism. The ability of oxygen and carbohydrate to reach the brain cell and their utilization in the cell determine the amount of cell activity as well as the life or death of the cells. The action of substances which increase the blood flow through the brain and which increase the carbohydrate metabolism have been reported, but just how these substances act, or fail to act, is not known. It has been taken for granted that anoxia is the cause of cell death and cell death the cause of many of the characteristics of senile psychoses(5), yet there are so many unknowns in the field of brain metabolism that this idea of the cause of brain atrophy is no more than an assumption, nor can we conclude that cell atrophy necessarily means psychosis.

Freyhan, Woodward, Kety, in 1951 studied the cerebral blood flow and metabolism in the psychoses of senility(6). They studied 10 cases with arteriosclerotic dementia and 5 cases with senile dementia (dementia without arteriosclerosis). They found a definite reduction in blood flow, with a concomitant decrease in brain metabolism. These investigators believe that the result was due to increased vascular resistance in these specific cases. Fisher(7) studied the

pathological findings in cases of senile psychoses. He thinks that the causative condition is always the same and would like to coin a new general term—"hypertensive arteriosclerotic encephalomalacia"—as he feels that there is always an increase in blood pressure, and also always arteriosclerosis. He admits that sometimes the arteriosclerosis cannot be found. He did find bilateral thrombosis of the carotid sinuses in 5 cases(8). He believes that extracerebral thrombosis may explain some cases of senile dementia thought to be due to primary cell atrophy. Thrombosis superimposed on arteriosclerosis seems to him to be the common lesion producing senile psychosis of all types.

Lipid metabolism, nitrogen metabolism, and carbohydrate metabolism have been studied in aged patients. In March 1954, Albanese *et al.*(9) reported that the utilization of glucose decreases with age. The utilization of fructose is only slightly affected. Invert sugar and sucrose are used more than dextrose. These authors suggest that fructose might be used to supply the carbohydrate needs of the brain cells in the aged.

It has been the custom to speak of long-lived families. It is also common knowledge that senile dementia tends to occur at about the same age in several generations of the same family. Yet until recently there has been no proof that inborn qualities as well as constitutional factors have much to do with the occurrence of senile change. Kallman and Sander(10) reported in 1949 on a study of 1,602 twin index cases over 60 years of age. They found that basic physical and psychological qualities which are similar tend to persist. They found "a variable capacity for survival." In other words, what was common to the twins was not certain forms of deterioration but a certain capacity of survival, which was held by certain similar characteristics. These findings suggest that we have been considering with great care those characteristics that deteriorate, while we ignore the qualities which survive. Perhaps if we studied these qualities we might be able to strengthen and broaden those qualities of survival which Kallman's studies indicate are inherited.

Psychological studies have substantiated many of the clinical findings of the psychia-

trist. There is a gradual loss of flexibility and of learning power as people age, which can be shown psychologically. Certain organic tests have been devised which the psychologist feels can indicate early senile change. Dörkin and Kral(11) in 1951 reported a psychological investigation in which they studied 31 cases of senile dementia and 4 cases of arteriosclerotic psychosis. The 31 cases varied in age from 66 to 86; the arteriosclerotic cases from 67 to 86 years of age. By means of numerous tests they reached a result, designated as the efficiency coefficient, for each individual. They decided that the process of senile deterioration does not depend on age. Also they found that the process was selective. The individual does not become senile in all traits. Some qualities are maintained in good order while others deteriorate. These findings strengthen the conclusion of Kallman and Sandor that the biology of senescence cannot be understood without consideration of the variable capacities for survival.

Psychiatrists have learned a great deal about treating the aged patient. They find that the depressive, the toxic, and the schizophrenic reactions found among the aged can be treated with success just as in a younger age group. They have found that many patients who seem to be hopeless victims of senile decay may respond to psychiatric and sociological therapy. On the other hand, the mere act of hospitalizing patients may be a risky business. The fate of the aged patient hospitalized for the first time was studied by one investigator(12). There were 2,883 patients over 65. The death rate in the hospital was 11 times greater than in the general population. Of course many aged people are sent to the hospital in serious physical condition, but this finding suggests that the separation produced by the act of hospitalization might be a threat to survival. Post(13) reports on the outcome of nervous breakdown in old age. He studied 214 cases—95 men and 119 women. Followed up 3½ years later, 56 patients had schizo-affective states and 158 were diagnosed as organic. The later studies showed that 27% of the functional cases were dead; 54% were discharged; while 60% of the organic cases were dead and 23% had left hospital. He

felt that the patient with a simple dementia had a poorer survival rate than a case of senile reaction complicated by a schizo-affective state. The presence of the neurosis or a psychosis could well act as defense against the dementing forces which surround the patient. Also the fact that the patient has the ability to act as a schizophrenic or as a depressed patient indicates that there must be a survival of potentials for further living. It might be well to consider the wisdom of removing a depressive reaction in the aged patient by electroshock. Perhaps we may in this fashion break down the last defense against senile psychosis.

In the sociological field the burden of our aging population has its most profound effect. It is here that community, state, and national efforts are being made to meet the socio-economic needs of the aged. The breaking up of the American family life has left the old mother and father, the grandmother and aunt with no place to go. It has been shown that lonesomeness, a feeling of not being wanted, and of not being of use in the world are definite factors in producing senile psychosis. Retiring from active life without having prepared something to retire into(14) is now recognized as a serious mistake. It is now also known to be a mistake to retire old employees because of their chronological age without consideration of the fact that the individual abilities are not determined by chronology. Undoubtedly infections and organic diseases of the heart, kidneys, bones, and joints have much to do with incapacitating individuals and with bringing on senile reactions. Proper treatment of the physical diseases of the aged as well as proper housing are now accepted as sociological steps worthy of state support(15).

In January 1954 Busse *et al.*(16) reported their study of 70 persons living in the community and 52 living in an institution. There was an average age of 70.9 years for the community series and 77.4 for the hospitalized group. Religious feelings do not increase with age, but become less strict especially as to dogmas. Sexual desire was maintained in 50%. Ability to fall in love and to desire marriage is common among people over 70; lack of sexual outlet produced more anxiety among the women than the men;

17.1% of the group did not get along with children. These investigators found that neurotic patterns caused handicaps as well as social and economic factors. They show that aged people have much the same needs, desires, and reactions as younger people, and although somewhat different they are important to understand.

The success of group therapies, of old age clubs, of community activities for the aged points to the social pathology of the old age group. Plato says, "He who is of a calm and happy nature will hardly feel the pressure of age"; and Cicero says, "Old men retain their intellects well enough if they keep their minds active and fully employed." These sayings of the wise men of the past are being proved in the laboratories of today.

There is evidence that inheritance is a definite factor in the selection of victims of senility. Therefore the only sure way to grow old gracefully is to be born into certain families that have the characteristics of longevity without senility. There is evidence that senile change parallels brain cell damage especially whenever there is lowered oxygen supply or deficient carbohydrate uptake. There is evidence that cerebral blood flow and cerebral metabolism are reduced in senile psychosis. This lowered metabolism is said by one to be caused by vascular constriction and by another attributed to arteriosclerosis with superimposed thrombosis.

Factors that narrow the individual's life also influence the occurrence of senility. Retirement, the exclusion of new interests, and finally the admission to a mental hospital all have a tendency to bring on deterioration and death; while new interests, increased human relations, and group activities seem to prevent the changing of normal senescence into senile psychosis. The development of a depression or a schizophrenic reaction in the aged has been shown to enhance their ability to survive. Would not such a reaction act as a new interest, even if a fantastic one?

Senility, therefore, is a disease of the older age group which may appear in any decade after the fifth, but has all the symptoms of a psychosomatic disorder. There are some factors that are inherited, some traits that depend on constitution. The nature of the blood flow to the cerebrum is the deciding

factor, but the quantity and quality of the effect on the cells may be determined by disease of the blood vessels but also by simple constriction. The blood vessel disease or the blood vessel constriction may well be part and parcel of a restricted life or a life which has become narrow and meaningless.

Persons over 70 have the same loves, the same hates, and many of the same needs as younger people. In the senescent there is a tendency to become more understanding and less rigid. Dogma and cant lose their value and superficialities lose their appeal. Loneliness, lack of responsibility, and a feeling of not being wanted all increase the restricted view of life which in turn leads to restricted blood flow. Loss of motivation and loss of reason for living are part of the psychological pathology of senility. The feeling of not belonging and of being excluded are portions of the sociological pathology as well as poor housing and poverty. As yet there is no laboratory proof of the parallelism but clinical experience demonstrates the relationship of these psychological and sociological factors to the cell death of the senile as well as to the vascular resistance which seems to cause it.

Little can be done about inheritance perhaps, and little more regarding the constitutional makeup of man, but much can be done in the psychological and sociological field.

Medical science has made it possible for a person to enter the later years of life with a healthy body unscarred by previous diseases. This same person can look forward to a life of accomplishments and satisfactions of a personal nature, and acceptance and approval in a society which offers security and understanding.

The pathology of senility is found not only in the tissues of the body but also in the concepts of the individual and in the attitude of society.

In summary, the exact causes of the change from normal senescence into senility are not known, but a great many studies are in progress. Each day brings forth some new knowledge from the busy laboratories devoted to study of the aging process. Kety has shown us that cerebral metabolism is reduced in the aged. Kallman has indicated that hereditary factors influence the survival

of qualities. It has been shown by others that senile change is irregular in its development so that the problem is to determine what potentials survive and to develop them to the utmost. More and more evidence is being brought forward to show that the senile change in man is a disease state arising from inherited, biological, psychological, and sociological causes. The pathology of senility exists in all these areas and it is by combining the efforts of investigators in each of these fields that at last we can learn how to prevent the disease.

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DISCUSSION

JOHN L. SMALLDON, M. D. (Brattleboro, Vt.).—Dr. Wilson's paper regarding the current knowledge of the physiology, the psychology, the pathological changes, and the social-economic problems of aging constitutes a distinct service. Although he states that the causes of senility remain an unsolved question and he denies suggestion of remedies, he has accumulated 8 challenging points.

1. The suggested use of fructose to supply the carbohydrate needs of brain cells in the aged.
2. The need for further research regarding the development of cerebral arteriosclerosis.
3. Qualities, perhaps inherited, which tend to

survive, require further study with the view of strengthening and broadening them.

4. Depressive, toxic, and schizophrenic reactions in the aged respond to psychiatric and sociological therapy.

5. Prolonged mental hospitalization may be a threat to the survival of the aged.

6. Steps should be taken to restore family life, or at least to develop more satisfying substitutes for it.

7. Study of the practice of basing retirement solely on chronological age is indicated.

8. A program of proper treatment of physical diseases of the aged requires further development.

The worker in the public mental hospital notes, often with surprise, that many senile patients, soon after admission, show marked physical and emotional improvement. We need to review present methods of care and treatment of our geriatric patients. Active therapy programs are indicated in place of purely custodial care. More than that, we need to develop plans for the early return of these patients to a more satisfying community environment, in order to take advantage of their capacity for resiliency.

Many states are establishing commissions to study such plans. Increasing numbers of physicians are becoming interested in the study of geriatric problems. One of the purposes of the A.P.A. Mental Hospital Architectural Study is to determine types of buildings and facilities best suited to promote this program.

A visit to the overcrowded and uncomfortable wards for the aged in most of our mental hospitals is a tragic experience. They sit lined up along corridor walls or in stilted rows in large, confusing groups, idle, hopeless, lonesome for familiar faces or suggestions of home. Small wonder that they rapidly deteriorate, physically and mentally.

Physiological aging and true organic deterioration may be largely irreversible, but the prominence of psychological factors in the illnesses of many make them amenable to therapy. Appropriate treatment necessitates comfortable, uncrowded, more home-like, and less confusing patient areas.

This problem is being attacked in a number of relatively new geriatric facilities. Last autumn at the Mental Hospital Institute, Dr. Maurice E. Linden excited a good deal of interest with his excellent presentation of the psycho-geriatric program at the Norristown (Pennsylvania) State Hospital. There it is being demonstrated that a full program of care and therapy of the emotionally ill aged patient, a program capable of operation because of the modern building designed for it, can produce worthwhile results.

Activity, re-socialization, and psychotherapy, as Dr. Linden has written, "may interrupt the degenerative process and allow for some degree of rehabilitation of the senile group to social usefulness." Lacking this result, the program frequently will produce "some return of self-sufficiency and independence, increased tranquility, and a potential for happiness."

CHLORPROMAZINE TREATMENT OF MENTAL DISORDERS¹

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Chlorpromazine,³ a derivative of phenothiazine, was developed in France by the Rhone-Poulenc Research Laboratories. Under its trade names of Largactil and Megaphon it has been the object of much interest and experimentation in Europe, during the past 2 years. In this country where it is known as Thorazine it has been accepted for its superior antiemetic properties. More recently it has been used in the treatment of psychiatric disorders.

PHARMACOLOGY

Courvoisier, *et al.* (1) have conducted extensive animal and chemical investigations and find that chlorpromazine exhibits the following properties: (1) Anticholinergic action; (2) antiadrenergic action; though there is no inhibition of the hyperglycemic response of adrenalin; (3) central effect which is sedative, anticonvulsive, hypothermic, and antiemetic. The drug is also said to lower the metabolic rate. (4) There is a mild antihistaminic and local anesthetic activity. (5) The compound potentiates certain drugs, especially morphine and barbiturate derivatives.

The fate of chlorpromazine in the organism is unknown but probably it is degraded in the liver (2). Little is excreted through the kidneys.

The work of Moyer, *et al.* (3) in this country indicates that chlorpromazine in dogs is a hypotensive agent which decreases peripheral resistance with a variable effect upon cardiac output. These authors found no evidence of acute renal toxicity, though parenteral administration increased sodium and water excretion.

¹ Read at the 110th annual meeting of The American Psychiatric Association, St. Louis, Mo., May 3-7, 1954.

² From the Department of Psychiatry, Baylor University College of Medicine.

³ Supplied through the courtesy of Smith, Kline and French Laboratories as Thorazine.

CLINICAL STUDIES

There appears to be considerable variability in the human response to chlorpromazine. The central depressant effects have been universally noted. There is usually a striking drop in blood pressure, particularly during the first few days of administration of the drug, with a compensatory tachycardia. Changes in body temperature, basal metabolism, urinary excretion have been variable. Other effects of sympathetic and parasympathetic inhibition have been noted. Increase of appetite may occur. No significant changes in the body biochemistry have been reported.

CLINICAL USES

Chlorpromazine has been used in Europe for a wide range of conditions in the fields of surgery, anesthesia, gynecology and medicine. It was introduced into psychiatry in combination with barbiturates in prolonged sleep treatment (4). Hamon, *et al.* first used chlorpromazine alone in the treatment of manic illness (5). Their good results were reproduced by Delay and his associates, who have treated a variety of psychotic patients with success (6). Of the increasing number of publications, mention should be made of that of Staehelin and Kielholz in Switzerland and more recently of Lehmann and Hanrahan in Canada (7, 8). Improvement, and often cure, has been described in practically every type of mental illness. As might be expected with a new therapy dosages and uses have differed considerably, but most authors have agreed that initial parenteral administration speeds up improvement. Treatment has been continued for months in some cases.

The present study concerns an unselected group of admissions to the psychiatric service of a general hospital together with a lesser number of outpatients, 95 in all. A majority of the patients received initially a minimum of 50 mgms. of chlorpromazine intramuscularly 4 times daily. The effects of the drug

are cumulative and it is usually possible to switch to oral dosage after a few days. Intramuscular administration is often painful and produces marked induration at the site of injection, particularly if the solution escapes into fatty tissue.

The total daily amount of chlorpromazine may be increased by as much as 100 mgms. *per diem* until optimum effect is achieved. Increasing familiarity with the effects of the drug has led to the use of higher dosages. In one case improvement was delayed until 1,600 mgms. a day had been given for 10 days. However the average therapeutic dose for psychotic patients is about 800 mgms. each 24 hours. In neurotic patients and in children treatment is started by the oral route and in doses as low as 30 mgms. daily. Once improvement was manifested medication was given solely by mouth and progressively reduced over a period of weeks. In a few patients who showed a tendency to relapse higher dosage was again instituted.

Although most of the expected clinical phenomena were observed during treatment there was a surprising inconstancy in degree in different patients. All the patients who responded to chlorpromazine showed an initial somnolence from which, however, they could be easily aroused. After the first few days of treatment the lethargy decreased. Some patients presented a rather striking similarity to patients a few days after prefrontal lobotomy—a fact remarked on by some of the European writers.

In spite of the lack of spontaneous activity, patients are fully oriented and even severely withdrawn patients showed a rapid increase in their contact with reality. Some said that they had never felt so relaxed and very few of the psychotic patients made any complaints about the treatment. Neurotic patients on the other hand were aware of the hypotension and described themselves as "light-headed, dizzy, and faint." None of the patients experienced frank syncopal attacks but these have been reported elsewhere(9). Some patients complained of a dry nose and mouth. Nausea and epigastric distress occurred occasionally in patients on oral therapy though this was somewhat unexpected in view of the well-established antiemetic properties. Three patients mentioned

aching eyes and experienced some difficulty in focusing on close objects. Occasionally injection is painful and in these cases procaine is added. While on intramuscular dosage many of the patients exhibited a marked grayish pallor which is quite characteristic.

The hypotensive response was always apparent, the systolic pressure often dropped by 40 to 60 points and diastolic reading by as much as 40 points. In no case was it found necessary to withdraw chlorpromazine on this account even in ambulatory patients. Two of the patients were hypertensive before treatment and in both of these blood pressure dropped to normal levels without bad effects. After the withdrawal of chlorpromazine the blood pressure returned to pretreatment levels within 48 hours.

The compensatory tachycardia is often conspicuous but does not worry the patients. One woman suffering from an anxiety state commented on it but said that it was not nearly as unpleasant as the palpitations she had experienced for years.

No consistent temperature changes were noted. A consistent reduction of body temperature did not occur. In 5 cases there was a marked elevation of temperature for a few days during chlorpromazine administration, without leucytosis or other clinical findings. These patients had few complaints and the pyrexia promptly subsided when chlorpromazine was discontinued. In 2 cases replacement of the drug was accompanied by return of the fever for a short time. Measurement of metabolic rate was not attempted but there was no clinical evidence of significant decrease. Increase of appetite was the rule and some patients became ravenously hungry and gained weight. This was true even where other signs of clinical improvements were meager.

Sleep was greatly improved in almost all the patients in spite of the fact that those on large intramuscular dosage were lethargic throughout the day. Improved sleep is often associated with heightened dream activity. It is worth noting that the total sedative requirements for the service have been greatly reduced since this new treatment was instituted. Also worth mentioning is the strange, striking quiet which has come over

TABLE 1
RESULTS OF CHLORPROMAZINE TREATMENT

	Total	In remission	Much improved	Slightly improved	Unchanged
Schizophrenia	29				
Paranoid		4	5	2	3
Hebephrenic		1	2	1	
Catatonic		1	3	1	
Simple					1
Unclassified		2	3		
Depression	18				
Manic depressive		4	2	1	
Reactive		1	4	2	1
With cerebral vascular disease.....		1			
Involutional melancholia		1	1		
Mania	2	2			
Anxiety State	9	2	4	3	
Hysteria	8				
Conversion		1	2	1	2
Dissociation		2			
Delirium	10				
Bromide		1			
ACTH		1			
Alcohol		5			
With organic brain disease.....		2	1		
Psychosis	2				
Unclassified			1	1	
Posttraumatic Neurosis	5		2	3	
Alcoholism	2		1	1	
Psychopathic Personality	2				
Aggressive			1		
Inadequate				1	
Emotional Immaturity	1				1
Neurodermatitis	1		1		
Childhood Behavior Disturbance....	3	1	1	1	
Narcolepsy (Idiopathic)	1		1		
Convulsive Disorder	2		1		1
Total	95	32	36	18	9

the ward with its population of acutely disturbed patients. On one occasion when supplies of the drug were exhausted this was brought home to us with particular emphasis.

When patients are on chlorpromazine the vital signs and blood pressure are recorded at 6 hourly intervals. All barbiturate sedation is avoided. When necessary, paraldehyde, whose action does not seem to be potentiated by chlorpromazine, is used for sedation. As part of an investigation into possible hepatic

toxicity many patients are given a battery of liver function tests before and every 4 days during treatment. Electrocardiogram and a thorough physical examination are prerequisites of treatment.

RESULTS

Table 1 briefly summarizes the results obtained to date with 95 patients. Many of these patients are still receiving chlorproma-

zine on an outpatient basis and are continuing to make progress. Some have been under treatment for over 3 months. Others have required but a few doses to relieve their major symptoms. In agreement with general experience states of psychomotor excitement and agitation have been quickly controlled with 200-400 mgms. daily. This seems to be true regardless of the type of psychomotor excitement. In one case of schizophrenic excitement, and one case of acute mania, however, chlorpromazine did not ameliorate the symptoms. The addition of 3 electric shock treatments on successive days produced a prompt remission in both these patients. This experience was duplicated with another case of involuntional melancholia. It seems as though the combination of EST and chlorpromazine does well in certain instances since all 3 of these patients had had previous attacks of lesser severity, which has required a greater number of EST's for improvement. Delirious states are notably responsive, often clearing up in a matter of hours. The series includes cases of toxic deliria due to alcohol, bromides, ACTH, and brain lesions.

The results in the schizophrenic patients have been gratifying, particularly in those with paranoid symptomatology. Of 14 paranoid schizophrenics, only 3 were not improved. Six of these have already returned home and are making good adjustments. In 3 patients with delusional ideas the hallucinations seem to have entirely disappeared. The following case history is illustrative:

A 32-year-old colored, married female was admitted because of combativeness, refusal to wear clothes, ideas of being poisoned, hearing persecutory voices, and generally disorganized behavior of 4 months duration.

Patient had an unhappy childhood and had always been introverted with compulsive habits, episodes of nervousness and severe dysmenorrhea. She was highly ambitious and never made friends, always hypersensitive and suspicious. Four months prior to admission the patient accused her husband and sister of trying to poison her, made violent assaults on her husband. She believed her mind was being controlled by others, heard voices plotting to kill her, was unable to sleep and refused to care for herself.

On admission she was acutely disturbed and presented a picture of paranoid schizophrenia. Physical examination was unremarkable and laboratory findings within normal limits. Her condition grew worse during first 4 days; totally disorganized in behavior with many paranoid ideas,

she was extremely belligerent. She was given chlorpromazine 50 mgm., I.M., q.i.d. After 6 days there was slight lessening of activity and paranoid delusions but she was still very disorganized, slept little, but ate better. Chlorpromazine was increased to 100 mgm., q.i.d. Within 24 hours there was marked improvement, she seemed euphoric, slept well, and ate with enormous appetite. There was moderate hypotension. Within 48 hours the patient was rational and cooperative, sleep rhythm was restored. Oral chlorpromazine was substituted after 4 days with continued improvement, and tapered off over the next 10 days. Patient continued to improve. She was discharged 23 days after admission in good health. She was friendly toward her husband, had no ideas of persecution or reference, showed good affect and had some insight into her illness. She has continued to do well at home.

All the cases of depression have shown some improvement and several have returned home and are doing well. Depressed patients, particularly those who showed much psychomotor retardation, did not demonstrate the striking results seen in the schizophrenic and manic group. However, improvement in depressed patients is often masked by the effects of chlorpromazine itself, and only when it is withdrawn or reduced in amount is the improvement apparent. The following case history is illustrative:

A 42-year-old married, colored man was well until 3 years ago, when he broke his ankle at work. Following this he was confused for 3 weeks and was thought by his doctor to have had a cerebral vascular accident. Since then he has been seclusive, nervous, and progressively more depressed, profoundly depressed in the past few months. He would not eat, slept little, cried, and read the Bible. He talked frequently of suicide, complained of backache. He had not been able to work.

On admission the patient presented a picture of retarded depression. Physical examination showed B. P. of 240/118 with hypertensive heart disease and grade ii retinal arteriosclerosis. Routine investigation and liver function tests were within normal limits. EKG showed left axis deviation; x-ray of spine was negative. Diagnosis was depression secondary to hypertension and possible cerebral vascular accident.

The patient remained depressed and almost mute for the first 10 days. During this period his B.P. dropped to an average of 210/110. Chlorpromazine was instituted, increased gradually by 50 mgm. steps each day up to 200 mgm. daily, by mouth (to avoid sudden hypotension). The patient improved at once; appetite increased and he slept well. He had no diurnal lethargy and was more sociable. Blood pressure dropped in 24 hours to 130/90 and in one week to 120/70. He was discharged 17 days later on 75 mgm. daily with B.P. 110/80. He was cheerful and considering a return to work. He had

no complaints referable to reduction in B.P. He continued to have backaches but did not spontaneously mention this.

Among the neurotic group response has been more variable. Most of the patients report some improvement but as mentioned above the side effects of chlorpromazine sometimes cause patients to refuse larger doses. The improved sleep habits and increased appetite in this group suggest that chlorpromazine would be of value as an adjuvant to psychotherapy. This case of conversion hysteria, though, appears specially noteworthy.

A 31-year-old married, white mechanic was referred because of painful paralysis of the left leg, nervousness and headaches of 3 months duration. His symptoms developed 30 minutes after a heavy truck transmission had fallen on his abdomen and left leg. His previous adjustment had been good though there were marital difficulties and he had been living for some months previously in a setting of tension on this account.

Following his accident he had been conservatively treated. Aside from the paralysis and extensive bruising there were no injuries. Neurological examination was negative except for stocking anesthesia of the lower extremity. He received osteopathic treatments and when these did not help was given a bad prognosis. After seeing several other medical men he was finally referred for psychiatric help by his lawyer. A diagnosis of conversion hysteria with tension state was made and psychotherapy instituted some 3 months after injury. Probably because of the compensation and legal issues the patient did not progress. Sodium amylal interviews were unrewarding. For over 5 months after his accident his leg was still paralyzed and very painful. He developed numbness in his right leg, was depressed, and losing weight. He entertained paranoid ideas against his physicians.

He was hospitalized and treated with chlorpromazine, 200 mgm. daily by injection. He became extremely drowsy for 24 hours. The next day he said that his leg no longer was numb and that he felt good. By the third day he was ambulatory with a slight limp. He was happy and elated over his improvement. He continued to improve while chlorpromazine was tapered off over a 2-week period. Three weeks after the termination of treatment he was back at work, eating and sleeping well. He stated that he had never felt so well in his life. He had fair insight into his illness and was unconcerned about the possible loss of a large financial settlement.

Two patients with convulsive disorder associated with behavioral disturbance are included in the series. One of these has fewer seizures with chlorpromazine than on any other anticonvulsant regime. This finding has been noted by others (10, 11).

Few undesirable reactions other than those attributable to the physiological effects of chlorpromazine have been encountered so far. Moyer, *et al.* in a study of renal and hepatic functions have found no evidence of toxicity in their patients who were, however, on smaller dosage. They also did not find abnormalities of the electrocardiogram or blood elements attributable to the drug. Lehmann and Hanrahan noted slight changes in liver function tests in some of their patients with clinical evidence of hepatic dysfunction in 3. In this series no conclusive evidence of hepatic toxicity has been found, even in patients with pre-existent liver damage of moderate degree. This aspect of chlorpromazine is being more extensively investigated.

Three patients developed more or less generalized skin eruption of an urticarial nature associated with malaise. More powerful antihistamines did not bring relief, but in each case cessation of chlorpromazine for a few days only allowed the skin to clear. One schizophrenic patient became very euphoric with outspoken erotic tendencies which subsided with discontinuance of treatment for 10 days. Two patients on high doses developed coarse tremor, muscular rigidity, and immobile expression. This Parkinson-like syndrome disappeared quickly after reduction of dosage.

There do not appear to be any absolute contraindications to chlorpromazine treatment. It should be used with caution in patients with hepatic, cardiac or renal disease and in those who have recently taken barbiturates or opiates.

COMMENT

Chlorpromazine has a diverse pharmacological action on the human organism. A considerable body of evidence has been accumulated pointing to its therapeutic efficacy in many kinds of mental disorders. It is a drug of low toxicity even in large doses and one which may be administered over long periods of time without an undesirable increase of tolerance.

It appears to be a highly effective agent for controlling psychomotor excitement of all kinds without the undesirable effects of the standard methods and maintaining the pa-

tient in a fairly accessible state at all times. Its action on other types of mental illness is not so remarkable but is certainly worthy of further investigation, particularly in the chronic schizophrenic patients in whom most treatments are unrewarding. Facilitation of communication together with a remarkable objectivity towards significant ideas and feelings has occurred in many of this group.

Speculation about the mode and site of action of the drug seems premature but such evidence as there is suggests that it is a subcortical one. While in the initial states of treatment there is a definite resemblance in the behavior of these patients to those who have been lobotomized there are none of the deficit found in the latter. Neither the dosage nor the mode of administration of the drug is in any way standardized. The initial results obtained in Europe and this country have been satisfactory enough to justify a thorough clinical investigation of chlorpromazine and a search for even more powerful related compounds.

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SLEEP LEVELS IN ENURESIS^{1, 2}

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Few psychiatric entities lend themselves easily to physiological study. Those that have a relationship to sleep have a particular significance. Nocturnal enuresis is one event the precise time of occurrence of which is easily recorded, and its relationship to sleep can be accurately determined. This paper will describe electrographic studies of the sleep levels and other physiologic changes prior to and during micturition in cases of nocturnal enuresis. These cases have been evaluated physically and psychiatrically.

The high incidence of nocturnal enuresis in childhood is recognized by the laity and the profession alike. Anderson(1) has cited figures of 10%-15% among all nervous children and 30% among institutionalized children. The strikingly high incidence among young adults is not so widely appreciated. According to Levine(2), 24% of naval recruits receiving neuropsychiatric discharges suffered from nocturnal enuresis, and 12 per thousand of *all* recruits had this difficulty. These latter figures are in agreement with our(3) findings on the west coast.

The frequency and incomplete understanding of the problem have been reflected in the wide diversity of etiological theories to be found in the literature(1, 4, 5, 6, 7, 8, 9, 10, 11, 12, 13, 14). Etiologies may, for simplicity, be divided into organic and functional. Setting aside that small percentage of cases having recognized neurological or urological pathology, we are left with the large group of "functional" cases to be explained. A few of the prevalent theories, such as hypersomnia, epileptic equivalence, neurological deficiencies, dissociative states, and emotional or ego disorders can be further evaluated by the methods of study to be described.

Our studies were made on 25 randomly selected male subjects, ranging in age from 5 years to 20 years. Twenty-two of these were naval recruits of 17 years or older. All subjects were studied physically, urologically, and psychiatrically. Continuous nocturnal electroencephalograms were recorded on all. To adequately monitor stages of sleep, electrodes were placed in the temporal, parasagittal-central, and occipital areas over the subdominant hemisphere. According to precepts well established in electroencephalographic experience (15, 16, 17, 18, 19), the following criteria were used for identification of the various stages of sleep: wakefulness—moderately continuous alpha rhythm, and complete freedom from slow waves (in adults); drowsiness—a loss of alpha activity and advent of random, irregular slow waves, especially anteriorly; light sleep—the appearance of "V waves" and 13-15 c/s spindling focal to the parasagittal-central area; deep sleep—random, high-amplitude delta waves, as strong in the occiput as anteriorly. Bed-wetting was signalled through one EEG channel by an electronic device sensitive to resistance changes. Recordings of EKG and EMG were obtained simultaneously by an electrode pair over the lower abdominal rectus muscle. These electrographic studies were repeated from one to two times in some of the cases.

The top half of Fig. 1 shows electrode placement for monitoring stages of sleep; temporal, central, and occipital over the subdominant hemisphere; and the circuit of the wetting indicator. The bottom half shows 3 samples of EEG tracings considered typical of states of wakefulness, light sleep, and deep sleep. The recording of the heart rate, and electromyogram of the rectus abdominis muscle is on line labelled EMG. The PGR line is the recording of the changes in the skin resistance due to the psychogalvanic reflex, which is considered to be one of the indications of the presence of anxiety, tension, or psychic struggle. The other indi-

¹ Read at the 110th annual meeting of The American Psychiatric Association, St. Louis, Mo., May 3-7, 1954.

² The views stated herein are those of the authors and do not necessarily represent the policies of the U. S. Navy or the Veterans Administration.

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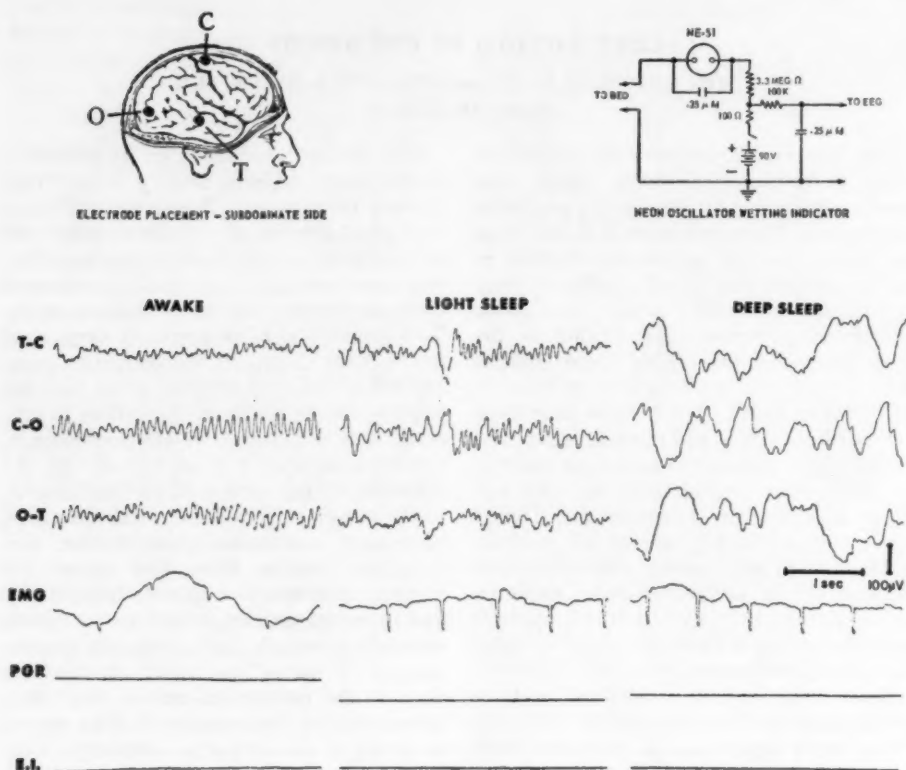


FIG. 1.

cations are changes in cardiac rate as recorded on line EMG, and evidence of temporalis muscle activity on lines T-C and O-T. The lower line of the 3 samples is labelled E-I, for enuresis indicator, and records wetting by rhythmic deflections of the line, as seen on the next slide. The indicator lags the onset of micturition by 6 seconds. A correction has been made in the samples.

A.J.—Figure 2 shows the EEG of A.J., age 5 years. The 4 samples show the waking tracing at the beginning of the test, light sleep, deep sleep, and the pattern at the time of wetting. Enuresis occurs during deep sleep. As there was no evidence of anxiety, EMG and PGR are not included.

E.U.—Figure 3 shows the EEG of E.U., age 7 years. The first 3 upper samples show the 3 stages of wakefulness, light sleep, and deep sleep, along with the heart rate. The fourth upper sample, labelled "Three Minutes Pre-wetting" shows the transition from deep sleep. Note the temporal muscle activity and the increased heart rate, from 76 to 100 beats per minute. The fifth sample shows

considerable temporal muscle activity, and even greater increase in heart rate, and, for the first time, skin resistance changes. The next sample is during wetting, and it shows all of the foregoing signs of tension; and in addition there is abdominal muscle activity, the significance of which will be discussed later. The third lower sample shows the

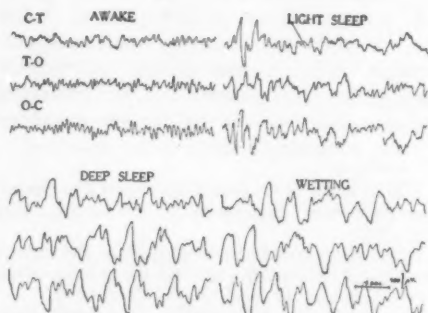


FIG. 2—EEG of A.J.

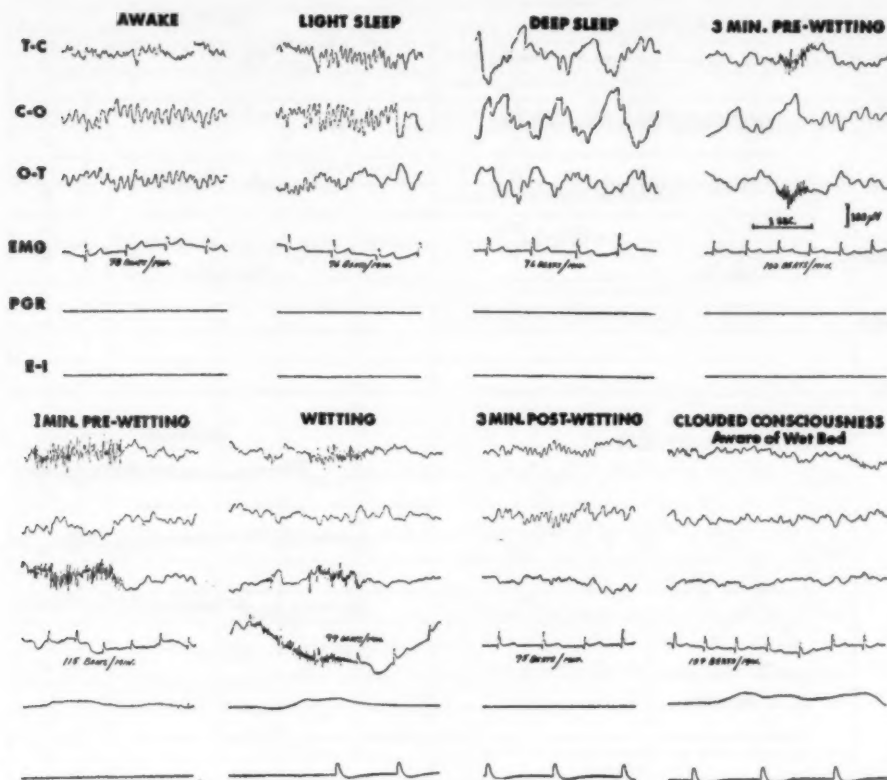


FIG. 3.—E.U.—7 yrs.

subject in light sleep 3 minutes post-wetting, with no muscle tension and the heart rate and PGR activity back to normal. The line E-1 continues to show the signal of the wet bed. The last sample shows the subject's response on being aroused and questioned as to the status of his bed. He was drowsy but oriented. The PGR is as active here as during wetting. In comparing the wetting sample with this and the other samples, it can be seen that the patient was in a mildly drowsy state during micturition.

Figure 4 concerns the same patient as Fig. 3, but the EEG done 1 year earlier at age 6. Here, he wets during EEG pattern characteristic of very light sleep. There are no signs of tension.

Figure 5 shows a typical pattern for 17 years and older. The first 3 samples show the usual arrangement. Wetting occurs during strong waking alpha, with evidence of psychic struggle in the form of temporal muscle tension, increased heart rate, and psychogalvanic reflex activity.

Figure 6 contains the data of the 25 cases studied. The subjects are arranged in order of increasing age and of increasing wakefulness at the time of wetting. With increasing age, there is a shift toward wakefulness and

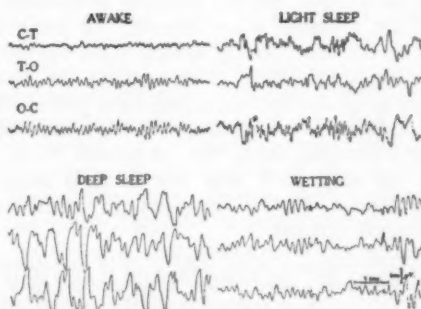


FIG. 4.—E.U.—6 yrs.

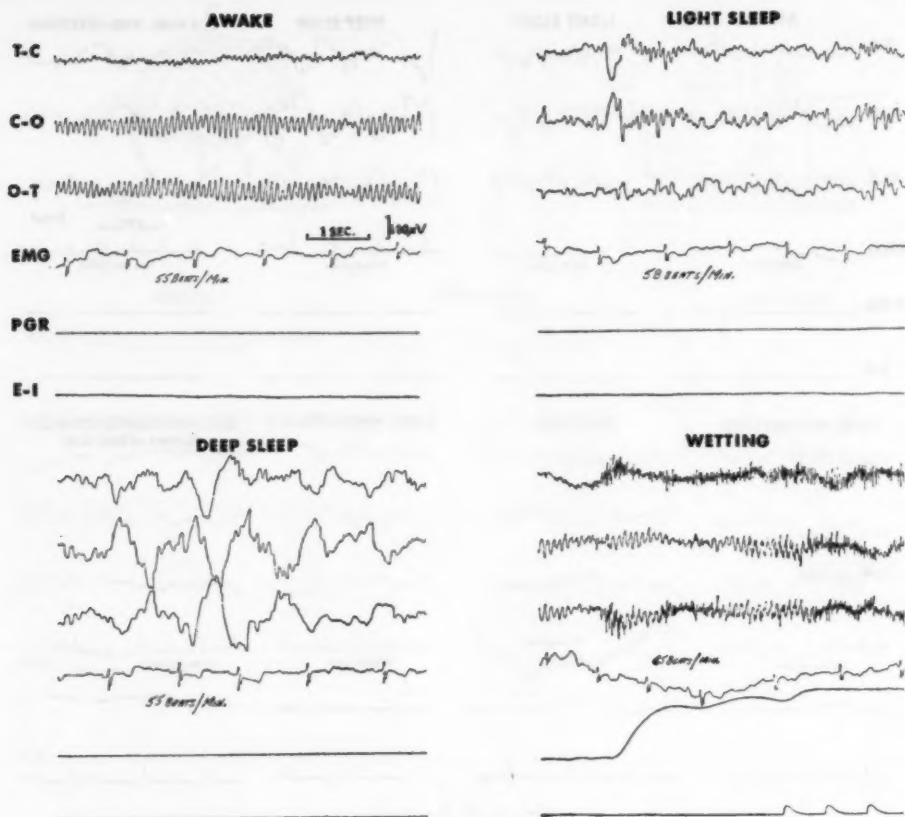


FIG. 5.—Adult.

a prolonged period of psychic struggle before micturition. An asterisk denotes that the patient remembered having had a dream during the study. The contents of the dreams indicate that they are conjoined to the act of micturition, but the temporal relationship of the 2 events is not known. All these 5 cases showed a strong waking alpha rhythm during micturition. The next to the last patient on the list had a prolonged period of wakefulness—30 minutes; he also suffered from somnambulism. The last patient, H. M., is the only adult who wet in deep sleep. Urological studies revealed a moderate urethral stricture.

H.M.—Figure 7 is the EEG of H.M. and shows wetting in deep sleep. There is no evidence of increased tension or abdominal muscle activity until later, when he has been awakened and is being questioned about wetting. Then, he shows a PGR re-

sponse, increased heart rate, and some temporal muscle tension.

DISCUSSION

1. All the subjects are known to be urologically normal and generally in good health, except for subject H. M.

2. There is no history of epilepsy in any of the subjects. The waking and sleeping EEG's are normal throughout, and in no case is there seizure activity or hypersynchronous delta or theta activity at the time of enuresis.

3. All the subjects reach a state of light sleep within 15 minutes, despite the novelty of the experimental procedure, the presence of electrodes on the scalp, and the strange environment. Except for one subject, all reached deep sleep within 55 minutes.

PATIENT	AGE	MINUTES TO REACH LIGHT SLEEP	MINUTES TO REACH DEEP SLEEP	SLEEP PATTERN BEFORE AND DURING MICTURITION	TENSION
AJ	5	8	30	DEEP SLEEP	NONE ↓
EU	6	9	30	LIGHT SLEEP FOR 1 MINUTE BEFORE	
"	7	12	25	DROWSY FOR 1½ MINUTES BEFORE	MODERATE ↓
JB	12	5	40	" " 5 " "	
WC	17	10	NOT REACHED	LIGHT SLEEP	* ↓
LC		7	25	DROWSY FOR 2½ MINUTES BEFORE	
VK		5	45	" " 4 " " - ALPHA AFTER	
RH		14	30	" " 3 " " - WAKING ALPHA WITH WETTING	
WE		14	35	WAKING ALPHA FOR 3 MINUTES BEFORE	
CB		6	50	STRONG WAKING ALPHA FOR 5 MINUTES BEFORE	
AM		9	30	" " " " 6 " "	
DB		5	50	" " " " 12 " "	
BR		4	55	" " " " 15 " "	
LF		6	30	" " " " 13 " "	
AC		10	25	" " " " 15 " "	
CW	18	5	55	" " " " 2 " "	
EM		15	45	" " " " 3 " "	
FB		10	45	" " " " 11 " "	
RT	19	15	50	" " " " 1½ " "	
HA		14	40	" " " " 5 " "	
CP		15	45	" " " " 8 " "	
JD		15	35	" " " " 9½ " "	
OL		5	55	" " " " 20 " "	
HB	20	10	25	" " " " 10 " "	
LR		5	50	" " " " 30 " "	
HM	17	8	25	(SOMNAMBULIST) DEEP SLEEP-TO LIGHT SLEEP AFTERWARDS - UROLOGIC PATHOLOGY PRESENT	NONE

* DENOTES DREAM

FIG. 6.—SUMMARY OF DATA ON 25 CASES

4. A few of the subjects were ostensibly difficult to arouse, even while the EEG showed a strong, continuous alpha rhythm and complete freedom from slow waves. In other words, some subjects were unresponsive to arousal stimuli at a time when the EEG pattern was identical to that in the full waking state; and when total orientation was finally achieved, there were no accompanying changes in the EEG. In most of the adult cases, the waking alpha was of high amplitude and almost continuous; drowsiness was immediately signalled by a loss of alpha activity. In the case of W. C., the null-alpha pattern started almost as soon as the subject got into bed, when he was still settling himself. Thus, the EEG evidence indicates that these several subjects were physiologically

awake at the time of enuresis, outward appearances notwithstanding.

5. Since Muellner's fluoroscopic studies (20), it is generally accepted that voluntary micturition is initiated by contraction of the abdominal and pelvic muscles to increase intra-abdominal pressure, and to depress the bladder neck. For this reason, the EMG electrodes were placed over the lower rectus abdominis muscle. Most of the adult enuretics who wet during alpha activity initiated the process by contraction of this muscle. Those who were drowsy also used this mechanism, but those in deeper sleep did not.

6. None of the subjects, on questioning, were aware of having wet the bed. They all either denied wetting or felt the sheets for confirmation. Yet, two of the adults called

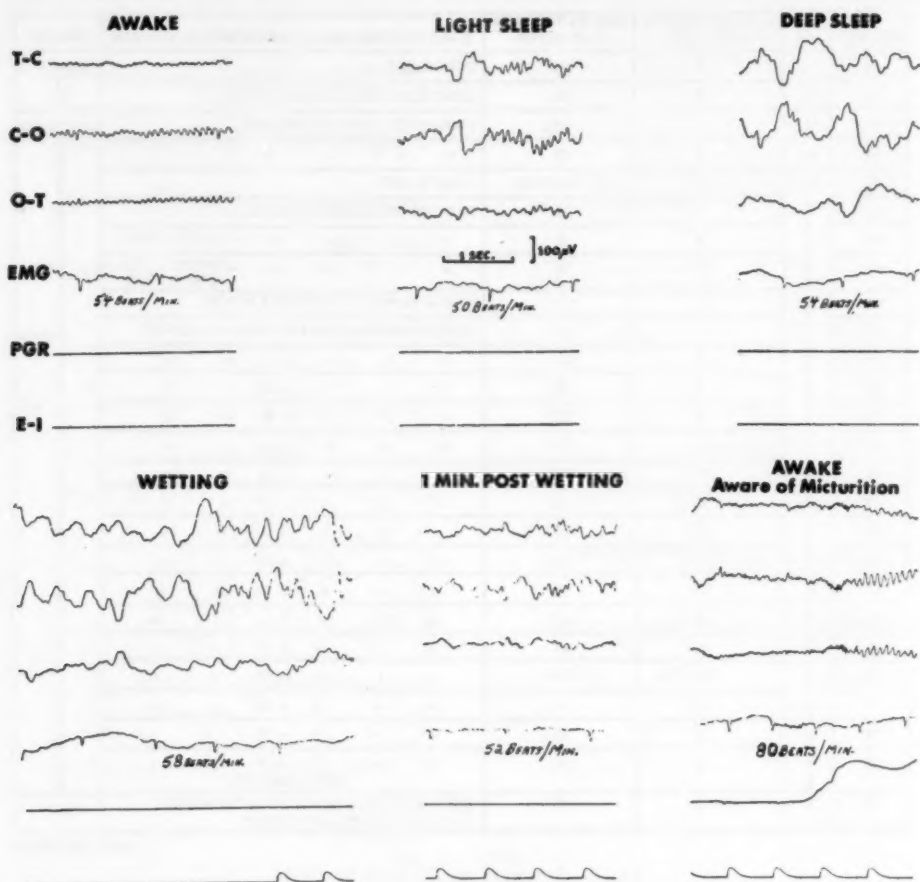


FIG. 7.—H.M.—17 yrs.

out to the doctor before urination, later denying having awakened. The findings of electrographic wakefulness before and during the act in these, and indeed in most of the adult cases, therefore suggest that they are in an hypnotic-like or dissociative state. The use of the abdominal muscles to initiate micturition strengthens this impression. At the same time, there is evidence that a psychic struggle takes place before and during wetting; there are increased EKG rate, muscular tension, and psychogalvanic reflex activity.

7. Our adult cases have thus impressed us with the importance of psychiatric factors in the explanation of persisting nocturnal

enuresis. Clinically, they are found to be poorly educated, poorly trained hygienically, usually of rural and large-family origin, and characterized by an immature, anxious, passive-aggressive personality. They conform with over 350 adult enuretics interviewed and evaluated psychiatrically by the authors(3).

CONCLUSIONS

In this paper, our series of cases is too limited to justify any extensive statistical treatment, but certain definite conclusions can be drawn about some features of nocturnal enuresis, and strong impressions may be cited about others.

1. Nocturnal enuresis is not a form of epilepsy and is unrelated to epilepsy except in those cases where it is really urinary incontinence accompanying a nocturnal convulsive episode.

2. Functional nocturnal enuresis is not due to excessively sound sleeping. For adults, at least, the evidence is to the contrary; although appearing to be hypersomnic, inasmuch as they resisted contact with reality, the majority of our subjects were physiologically awake at the time of bedwetting.

3. Bedwetting may occur at any stage of somnolence, from deep sleep to wakefulness; but our findings suggest that the more automatic variety, during deep sleep, is relegated to the early years of childhood. It is possibly due to delayed maturation of neural pathways. With the approach to adulthood, the spectrum of sleeping states rapidly shifts toward wakefulness, and the problem becomes increasingly a psychopathological one. This adult type of enuresis, we are impressed, should be viewed as a dissociation or repression phenomenon. By the methods we used to measure tension or anxiety, we found that it is not eliminated by this psychic mechanism, but it may be reduced. It would seem that the mechanism allows the individual to solve his problem of a full bladder and to save his conscience from knowledge of the act; but this gratification is not purchased without some payment in the form of anxiety at the time.

4. The EEG can be used as a diagnostic aid in enuresis. The procedure is not formidable; it is little more than a sleep EEG. How soon one micturates is a function of the amount of water taken, and this amount can be set to produce a full bladder in 55 minutes, i.e., during deep sleep. The fashion in which the problem is handled can then be ascertained.

5. For treatment, psychotherapy seems indicated in those cases showing dissociative behavior. Drug therapies, such as the use of atropine or pitressin, delay the filling of the bladder and are therefore only symptomatic treatments. The conditioned-reflex treatment has the disadvantage of associating waking with a post-wetting state. This deficiency could be overcome, at least in cases of dissociative enuresis which have strong, per-

sistent alpha activity. The appearance of the alpha rhythm might be used to trigger an arousal stimulus by means of an alpha frequency filter-integrator, in a manner suggested by Offner (21). Thus, the conditioned awakening would be associated with the stimulus of the full bladder.

To summarize briefly, nocturnal enuresis can occur at any level of sleep. That of the more adult ages, for the most part, occurs during physiological wakefulness and for this type the diagnosis of dissociative reaction is indicated. An electrographic method that can be used diagnostically in enuresis is offered. This method also may be used further to study the relationships of sleep, dreams, anxiety, enuresis, and the formation of dissociative states.

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DISCUSSION

PAUL W. DALE, M.D. (Phoenixville, Pa).—I would commend this piece of research because it is a beautiful demonstration of what is known as the *scientific method*. The authors set before themselves the task of determining the depth of sleep at the time of enuresis. So far as I know, this has not been worked out before. My cursory examination of the literature revealed considerable inconsistency of opinion on this subject with the frequently expressed opinion (only a hunch) that enuresis occurs during deep sleep. We find this afternoon that this particular hunch was not correct.

To recapitulate briefly, Doctors Ditman and Blinn have told us that little children wet their bed without waking up; but that after toilet training is well established, enuretic older children and adults *do* awaken or become nearly awake before wetting their bed and at the same time show somatic changes, such as increased pulse rate and increased muscle tension. At least this was the case in those individuals studied by the authors.

This brings us to that damnable problem of: What is necessary for good control of an experiment? We hear a lot these days about the need for controlled experiments. We have heard a lot about controls at this meeting. It seems that discussants talked about it more than authors. Is this because discussants know more about what constitutes good control than authors? I think not, for next year we shall find that many of this year's authors are now discussants talking about control. I think it is because a discussant must not show an altogether uncritical acceptance of a paper or the audience might feel that he had hardly read the paper, or only in a cursory manner. To talk about controls is very easy because no piece of investigation can be 100% controlled; however, I would caution you not to close your mind to pieces of work that do not have experimental controls. The famous experiments of William Beaumont were reported for the most part without the benefit of control. Dr. Beaumont did not have the modern day notion of a statistically valid series; nor did he check, in a detailed way, all the variables of his experiments. Yet his findings were very beautiful and greatly contributed to our knowledge of physiology. It is

this beauty of results, this excellence of pattern, this nice way in which the jigsaw puzzle fits together that after all leads us to the acceptance of a piece of research, more than the rigorousness of the controls. The findings of Doctors Ditman and Blinn have this satisfying beauty of results.

I might mention the points of incompleteness. First, the series is small. We should be cautious in generalizing from so few to so many, particularly in view of the known variability of human behavior. Second, it is not to be presumed that an individual, hyperhydrated, lying on a cot in a laboratory, and hooked up to a great number of different wires can be expected to sleep and enurese⁵ in the same fashion that he would in the comfort of his home and inner spring mattress. All of this is but a general statement that to observe is to alter the thing observed. This problem is common to most fields of science, although the astronomers seem to safely escape it. In other words, Drs. Ditman and Blinn had to do something to their individuals in order to find out something about them; their test persons were not the same individuals as before. This paper should perhaps be entitled "Sleep Levels in Enuresis in Hyperhydrated Subjects Who Are Taking Electroencephalograms, Etc." Notwithstanding these objections I would say that everything Drs. Ditman and Blinn have told us fits together so beautifully that I think we can safely conclude that toilet-trained individuals *do* become awake or nearly awake and *do* show somatic signs of distress prior to wetting their beds, while non-toilet-trained individuals are able to enurese without waking up and without becoming distressed. It must be, then, that the introjected effects of the toilet training can enter the neuronal network of our subject's central nervous system when the sensory stimulus from the full bladder signals that the organ is distended. Then the effects of this training inhibit the automatic reflex micturition and instead set up discharges in the reticular substance of the midbrain, or wherever the set of alertness is, and wake the patient up. By then other forces of the personality assert themselves, and the subject wets the bed anyway. Thus, enuresis of the type studied by Drs. Ditman and Blinn is neither a neurologic nor urologic problem, but one for the psychiatrist or others who know how to deal with this and similar intrapsychic conflicts and irregularities of behavior.

⁵ This word is not in Webster's Dictionary but the meaning of this verbal form is obvious.

EXPERIMENTAL STUDIES ON ANXIETY REACTIONS^{1, 2}

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INTRODUCTION

This report deals with observations of man's attempts at adaptation in experimentally induced and naturally occurring situations (1-17), with particular emphasis on stress-induced anxiety. The following definition of the term "anxiety" is used: a feeling of apprehension in response to danger which threatens the integrity of the individual. This state is accompanied by alterations in one or more physiologic variables, which may differ in degree, integration, and duration among individuals and in the same person from time to time.

In this study techniques from the physiologic, psychologic, and sociologic disciplines have been employed (18-27). No uniform method has been applied to all observations. Rather, each experimental situation was evaluated in context by the method or combination of methods deemed most likely to yield information pertaining to the question asked. No attempt has been made to include illustrative examples of all the psychophysiology and psychosocial correlates of anxiety. Rather, selected data have been organized into a frame of reference designed to emphasize the relevance of anxiety to man's attempt at the maintenance of homeostasis and the natural history of illness.

ANXIETY, SUSTAINED MUSCLE CONTRACTION, AND BACK PAIN

The importance of the role of the autonomic nervous system in anxiety reactions

previously has been reported (5-16). It should also be emphasized that the somatic nervous system which regulates the function of structures under conscious control also plays a part in anxiety (4, 28).

A 32-year-old white Roman Catholic housewife and part-time nurse of German extraction complained of pain of 5 years duration in the lumbosacral region. Action potentials were recorded from the back muscles as the subject discussed her unhappy childhood. She lay rigid and motionless on the table, giving free expression to her intense anxiety commingled with feelings of resentment, humiliation, and guilt. When increased electrical activity had been sustained for 6 minutes, the subject noted the onset of a backache which persisted for 30 minutes. The conversation was directed to neutral topics and the patient immediately became relaxed and at ease. The pain promptly disappeared as the increased electrical activity and muscle tension subsided. Eight and a half minutes later the conversation about personal problems was resumed. Both sustained muscle tension and increased electrical activity reappeared, and one and a half minutes later the patient again complained of back pain. She was then diverted and reassured and once again she became relaxed. The muscle tension and electrical activity from the muscles subsided, and the pain disappeared.

Comment.—The genesis of the pain in this anxious subject is dependent on the circulatory and metabolic dynamics of skeletal muscle activity (28). The actual process of contraction, by obstructing mechanically the arterioles supplying the muscles with blood, renders the muscle relatively ischemic for the duration of the contraction. The degree of ischemia is roughly proportional to the contraction strength, a strongly contracting muscle being almost completely ischemic. Thus, depending on the form, duration, and intensity of motor activity, the muscle may be relatively ischemic over a long time interval. This prolonged state of anaerobic activity allows for the accumulation in the tissues of metabolic products which would otherwise have been dissipated in the presence of adequate blood flow. These noxious metabolites constitute the critical stimulus for the pain in the backache syndrome. The available evidence indicates that muscle potassium is the pain factor or one of its important components (29).

¹ Read at the 110th annual meeting of The American Psychiatric Association, St. Louis, Mo., May 3-7, 1954.

² This project has been supported in part by the State of Washington Research Fund under Initiative 171; by the Harry J. O'Donnell Psychiatric Research Fund; by the Medical Research and Development Board, Office of the Surgeon General, Department of the Army, under Contract No. DA-49-007-MD-396; by the Institute of Mental Health, U. S. Public Health Service; and by the U. S. Air Force under Contract No. AF18(600)-425.

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URINARY 17-KETOSTEROID EXCRETION DURING PERIOD OF ACUTE ANXIETY

The subject was a tense, anxious, and insecure 29-year-old white male physician. Comparison is made between 2 days, of what were for him a period of relative comfort and productivity, and one day of intense anxiety with grossly impaired productivity. On December 8 and 14, the days of relative security, the subject's 24-hour excretion of 17-ketosteroids was 43.05 mg. and 43.83 mg. respectively. The fractional values for December 8 were: morning, 2.39 mg./hr., afternoon 1.907 mg./hr., evening 1.59 mg./hr., night 1.62 mg./hr.; and for December 14: morning 2.60 mg./hr., afternoon 2.26 mg./hr., evening 1.48 mg./hr., and night 1.47 mg./hr.

On the day of stress the subject found himself confronted with an overwhelming work schedule. He was anxious, tired, irritable, and preoccupied with personal conflicts evolving from the current phase of his psychoanalysis. He was tense and restless and noted a persistent twitch involving the left eyelid. He felt dissatisfied, and his difficulty in concentration was associated with low productivity. Despite his mounting fatigue and poor effectiveness he drove himself at his work until midnight. Sleep was punctuated with frequent anxiety dreams. Total 17-ketosteroid excretion for this day was 87.25 mg. Fractional values were uniformly elevated over comparable times on the control days, with the night sample containing the greatest amounts: morning 3.24 mg./hr., afternoon 3.54 mg./hr., evening 2.54 mg./hr. and night 4.66 mg./hr.

Comment.—In general, variations in urinary excretion of 17-ketosteroids observed in a variety of experimental situations appeared to be directly related to the need of mobilization of bodily resources for action.

It is postulated that: (1) the alterations in the excretion of 17-ketosteroids observed were an index of the amount of adrenocortical hormone produced; (2) during action, tissue utilization of adrenocortical hormones occurs in skeletal muscles and is roughly proportional to the form, intensity, and duration of the activity.

In settings of security, taking action was associated with a moderate decrease in excretion of 17-ketosteroids. In settings of competitive reactions or intense feelings of anxiety, tension, or hostility, taking action was associated with sustained or slightly elevated 17-ketosteroid excretion. If, in such a setting, action was not taken, there occurred marked elevations in excretion of 17-ketosteroids. Exhausting action (heavy exer-

cise) regardless of affect or life setting was invariably associated with a profound decrease in excretion of 17-ketosteroids followed by a marked rise during the recovery period. When taking action did not appear to be required by the threatening situation and the ensuing inactivity was not accompanied by overt anxiety and tension, there was a decrease in excretion of 17-ketosteroids.

NASAL AND GASTRIC FUNCTION DURING ANXIETY

The following observation made on an adult male subject with a large gastric fistula documents alterations in 2 physiologic systems participating simultaneously in anxiety states (2, 30). It is also illustrative of variations in function of the same system at different times. As will be noted, the way in which the subject perceives the stimulus situation, and reacts to it are different for each occasion (31).

The subject was obliged to remove from a laboratory cage a rat that had been dead for some hours. In the cage were a number of living rats who had macerated the cadaver. He was obliged to put his unprotected hand into the cage, and in spite of his experience he had fears of rat bites and their implications. Furthermore, the cannibalism of the rats and the decayed condition of the malodorous cadaver gave rise to nausea. He experienced intense apprehension and disgust. Both his gastric and nasal mucosae became pale and stayed so for several hours.

At the time of the next observation, the subject's wife was about to visit the hospital because of troublesome varicose veins. His concern about hospitals and sickness and his dependence upon his wife for the proper conduct of the home engendered conflict with feelings of anxiety and resentment. Hyperemia and engorgement were noted in both the gastric and nasal mucosae.

EARLY CONDITIONING EXPERIENCES AND THE GENESIS OF ANXIETY

Infants with excessive crying during the first 3 months were investigated and compared with noncrying infants (32). The babies with excessive crying had anxious, unsmiling facial expressions and during crying displayed considerably more frenzied motor activity, wheezing, and sweating than did the noncrying group. Regurgitation and

passage of flatus often occurred toward the end of a period of excessive crying.

Upper gastrointestinal roentgenograms were done at 5 to 7 weeks of age. In all instances the films of the crying children revealed excessive gas and more rapid stomach emptying than occurred in the noncrying group. The crying infants showed wide fluctuations in absolute eosinophil counts ranging from 0 to 1442/cu. mm., while counts in the non-crying babies were stable within the normal range. Elevations of eosinophil levels occurred within 15 minutes after beginning of crying, and persisted, with the excessive crying, for as long as 2 weeks. Hyperemia, hypersecretion, and swelling of the nasal mucous membranes appeared earlier and were sustained at greater magnitude in the infants with excessive crying(2). The crying babies had increased muscle tension when awake. As determined by the Wetzel Grid growth rate increased during the 3-month crying period(33). The excessively crying babies had significantly more illness than did the non-crying infants. These included upper respiratory infections, skin rashes, diarrhea alternating with constipation, regurgitation, and accidents.

Excessive crying most commonly occurred in settings of domestic conflict and tension arising from the parents' attitudes toward their infant and problems in social and interpersonal relations. In the earliest neonatal relationships the parents of the crying babies were insecure, anxious, tense, and unable to achieve satisfaction from their performance. The mothers were strikingly inconsistent in the frequency, duration, quantity, and quality of handling and feeding, and in the length of time allowed to elapse before responding to the infant's cries. These mothers were unable to make discriminating judgments concerning their infant's communication and their attempts at child care were often unrelated to the child's needs(34). The crying, by provoking or increasing the mothers' anxiety, tended to establish a vicious circle, the parents' behavior becoming more inappropriate and the infant's crying more aggravated. It was in such settings that the physiologic variables of the infants showed fluctuations of the greatest magnitude and duration and that illness was most apt to occur. By contrast, the parents of the non-crying babies were consistent in the application of their techniques of child care and their assessment of the infant's communication.

Comment.—In the first month of life crying in both groups of babies persisted until individual needs were satisfied. After about 6 weeks of age the 2 groups were distinct. The noncrying infants were relaxed and happy. Crying, when it did occur, stopped promptly with the presence of a parent or other adult. The success of this adaptive behavior appears related to the regular and appropriate need satisfaction

which characterized the previous experience of the noncrying infants. Infants in the high crying group at the same age were tense, restless, and irritable. The presence of a parent or adult commonly initiated or enhanced the crying. It appears that because of their early conditioning experiences these infants failed to associate mother's presence with satisfaction and security. Rather, the parents' communication actually connoted danger, frustration, or deprivation to the baby and provoked a reaction of anxiety manifested as crying with its physiologic concomitants. These inferences are in agreement with those of Benedek(35, 36) and Freud(22).

ANXIETY STATES AND DISEASE

The evidence thus far adduced indicates that threats of danger due to stressful life situations may become important in the genesis of illness. Often the discomfort and tissue damage evoked by symbols are indistinguishable from that produced by physical and chemical agents or infectious microorganisms. It, therefore, appears relevant to an understanding of the natural history of disease to consider the effects on bodily integrity of the interaction of multiple noxious stimuli applied simultaneously.

EFFECTS OF ANXIETY-PROVOKING STIMULI INTRODUCED DURING EXPOSURE OF HAY FEVER PATIENT TO POLLEN(3)

A 57-year-old housewife born in the British West Indies of mixed Negro and white stock complained of "hay fever" of 5 years' duration and had a strongly positive ragweed skin test.

The experiment was performed during the hay fever season while the subject was feeling calm, secure, and relaxed. She was free of hay fever symptoms, and her nasal mucous membranes appeared moderately red with small amounts of secretion and swelling apparent. She was then exposed in the experimental pollen room for 109 minutes. Mild symptoms of rhinitis and low grade nasal hyperfunction ensued within 30 minutes. These symptoms subsided after 8 minutes and aside from some nasal obstruction the patient remained comfortable for the next 10 minutes.

At this point an interview was begun which the patient quickly directed toward the unsatisfactory relationship which existed between her husband and her second daughter. As she discussed this she became tense and anxious and her voice became whining and petulant. Examination revealed a

marked increase in the nasal hyperfunction. At the same time, increased symptoms of rhinitis recurred.

After this problem had been discussed for 33 minutes she was diverted to neutral topics and felt much reassured. Gradually over the next 28 minutes she regained her feelings of well-being, and despite the fact that she was still being exposed to pollen in the pollen room, nasal hyperfunction subsided, symptoms disappeared and she remained comfortable for the duration of the experiment.

Comment.—It has been demonstrated repeatedly (2, 3) that the alterations in nasal function accompanying conflictual settings are often sufficient to produce troublesome nasal symptoms and pathologic tissue changes. Also from a study of the histories of patients exhibiting common nasal disorders and from observations on individuals followed over long periods, it has been possible to establish a correlation between a setting of conflict with anxiety and nasal hyperfunction and an exacerbation of nasal disease. Further, since conflicts evolving from difficulties in interpersonal and social adjustments often remain unresolved for long periods, the accompanying anxiety and nasal hyperfunction may become both intense and sustained. In such a setting the nasal tissues become unable to tolerate the additional alterations in nasal function engendered by new threats or assaults on bodily integrity. Thus, the nasal hyperfunction appearing as a part of an individual's response to a threatening life situation causing conflict and anxiety may constitute a major etiologic factor in nasal dysfunction. When combined with other environmental stimuli capable of producing nasal hyperfunction, it becomes relevant to the genesis of many common acute and chronic disorders of the nasal and paranasal spaces.

ANXIETY AND PRE-EXISTING DISEASE

Regardless of the nature of the etiologic factors, a disease process, once established, constitutes a new stimulus situation, which in turn may initiate inappropriate and costly reactions. In the following observation an attempt has been made to explore the significance of anxiety appearing during the course of a well-established disease process.

The subject was a 55-year-old Greek male who had been admitted to the hospital 3 months previously complaining of left lower quadrant pain.

The extensive diagnostic procedures carried out during the interim had failed to reveal the cause of the pain. The patient became progressively discouraged and anxious and, as his discomfort increased, he complained bitterly about "being neglected" and was continually concerned with "what was going to happen" to him. At the time of the following experiment he appeared chronically ill and had a decubitus ulcer on the right hip. His communication was that of anxiety and depression, and he complained freely of generalized abdominal and back pain of steady, dull, and aching quality. Examination revealed considerable muscle spasm of the abdomen and the strip muscles of the back. The abdomen was tender throughout but more so on the left side. Tenderness of the back muscles was striking, being most prominent in the left lumbar region. Firm pressure over these "trigger areas" not only increased the pain in the back but also in the left lower quadrant of the abdomen.

At this point, as the examiner reassured him, the patient was given 0.25 gm. of sodium amylal intravenously. He promptly became relaxed and calm and the pain completely subsided. Examination revealed the muscles of the back and abdomen to be relaxed with only moderate tenderness to pressure. Pressure over the tender areas in the back caused no radiation of pain into the abdomen. Palpation of the relaxed abdomen revealed a moderate sized mass in the left upper quadrant, found at operation to be a hypernephroma. Manipulation of the mass caused intense pain to which the patient reacted with overt anxiety and agitation. He was again reassured and gradually the pain subsided.

Comment.—It is apparent from this observation that the tumor involving pain-sensitive structures was not the only source of discomfort. The complete subsidence of pain following the dissipation of anxiety and skeletal muscle tension by the sodium amylal indicates that the skeletal muscles were a major source as well (4, 7, 15, 28). On the other hand, pressure or displacement of the abdominal mass was necessary for the production of noxious sensations from the pain-sensitive structures involved by the new growth (37).

The following rationale for these observations is offered. As a result of the barrage of impulses arising from the pain-sensitive structures in the new growth, 3 reactions were set in motion: local spinal cord reflexes leading to segmental skeletal muscle spasm, the genesis of secondary hyperalgesia involving segmentally both superficial and deep pain-sensitive tissues (37), and the genesis of anxiety as part of the patient's total reaction to a threatening situation of which pain was

only one component. The additional skeletal muscle tension caused by the anxiety became the secondary pain source (4, 28, 38). The pain from the sustained skeletal muscle spasm, by perpetuating the anxiety, initiated a vicious cycle which also perpetuated the discomfort even in the absence of constant pain from the hypernephroma.

ANXIETY, DISEASE, AND SOCIAL PERSPECTIVE

CULTURAL CONFLICT AND TUBERCULOSIS (17, 39)

Psychosocial data have been obtained from a representative sample of approximately 1,000 patients with tuberculosis drawn from the metropolitan area of Seattle, Washington. The subjects were 70% male, 22% nonwhite, and 61% unmarried. The median age was 41 years with 64% older than age 35. When compared with the 1950 United States census figures for Seattle (50.1% male, 5.9% nonwhite, 34.8% unmarried, median age 34.4 years, 55.4% age 35 and over), the tuberculosis group represents a marked variation in character of population. Income and education also deviated from the urban median and was more like that of the rural population of the state. Only 11.5% of the patients earned \$4,000 per year or more compared with 43.8% in Seattle and 15.9% for the state. The median level of education for patients was 10.9 years. For Seattle's population the median educational level was 12.1 years, for rural nonfarm it was 10.2 years, and for rural farm 9.2 years. The white patients tended to be first or second generation Americans and hence originated from divergent cultural backgrounds to a greater extent than the majority of the population of the city. Over half of the patients had migrated to the city from rural areas. High frequencies of residential and occupational mobility and social isolation completed the pattern of nomadism for the males. The females had almost invariably engaged in productive work and 75% were employed at the time the disease was discovered.

Additional social perspective was provided by ecologic studies on all the 481 newly detected cases of active tuberculosis in Seattle in 1952: 269 white males, 88 white females,

88 nonwhite males, and 36 nonwhite females. Utilizing census tract data, the city was divided into 4 relatively distinct socio-economic residential areas: Area I included the city center and Seattle's "Skid Road" population, Area II the "working-class" population of the city, Area III the typically "middle-class" population, and Area IV included Seattle's "well-to-do" population. Tuberculosis rates per 100,000 population were analyzed by area of residence, age, sex, and race (see Tables 1 and 2).

Rates ranged from significantly high in Area I to significantly low at the periphery (Area IV), irrespective of age or sex. The nonwhite rate, however, was highest in the better socio-economic area at the city periphery. Diagnostically, far-advanced tuberculosis was the mode for Area I, moderately advanced disease for Area II, and minimal tuberculosis for Areas III and IV.

Life history data revealed the tuberculosis subjects to be sensitive, anxious, rigid, and emotionally labile. These patients, when compared with the cultural norms, were marginal people at the time of onset of tuberculosis. They started life with an unfavorable social status and grew up in an environment that was for them crippling.

TABLE 1

TUBERCULOSIS ATTACK RATES PER 100,000 BY SEX AND AGE, FOR SEATTLE AREAS, 1952

Area	Male		Female	
	To age 29	30 and over	To age 29	30 and over
I	188	616	239	159
II	73	297	56	85
III	41	176	40	41
IV	27	114	33	39
Total	150		53	

TABLE 2

TUBERCULOSIS ATTACK RATES PER 100,000 BY AGE AND BY ETHNIC-SEX CATEGORY, SEATTLE AREAS, 1952

Area	Age Range		Ethnic and Sex			
			White		Non-White	
	Under age 30	30 and over	Male	Female	Male	Female
I	189	457	482	140	762	535
II	53	196	166	49	481	275
III	39	105	91	29	468	276
IV	28	71	57	32	1,137	569
Total ..	44	146	83		347	

They were, in essence, strangers attempting to find a place for themselves in the contemporary American scene. As perceived by the individuals with tuberculosis, the poorly understood world in which they lived was a source of perennial danger and the threat of being "walled off" and rendered "helpless" was always imminent. The nature of their attitudes and life experiences made it unusually difficult for them to decide what was expected of them or what they expected of themselves. As a consequence their attempts at adjustment were characterized by unrealistic striving which was not only unrewarding but also productive of cumulative conflict, anxiety, and depression.

Disintegration of the patient's precarious psychosocial adjustment almost invariably occurred in the 2-year period preceding the onset or relapse of disease. The manifestations of the life crisis that ensued included high frequencies of broken marriages and changes in residential and occupational status. Alcoholism, frequent and persistent psychosomatic disorders, and mental illness were common. It was in this setting of increasing life stress acting on individuals whose limited capacities were no longer adequate for resolving problems or achieving satisfaction that tuberculosis apparently developed.

Comment.—In keeping with other investigations of the relationship of the social process to illness (40-52), these psychosocial data indicate that cultural conflict and anxiety contribute significantly to the natural history of tuberculosis. The consequences of ethnic, racial, and economic minority status and the processes of urbanization and industrialism are clearly evident.

PSYCHOPHYSIOLOGIC REACTIONS AND TUBERCULOSIS (1)

Since it has been demonstrated that adrenal hormones influence resistance in tuberculosis (53, 54), the relationship of life stress and adrenocortical function in these patients was investigated. Patients with pulmonary tuberculosis exhibited widely fluctuating 17-ketosteroid excretion patterns ranging from 2.0 mg./24 hrs. to 30 mg./24 hrs. A majority of the patients demonstrated excretion levels below the normal expected for their age and sex (55-58).

Chest X-rays revealed that patients with reduced 17-ketosteroid output had extensive and exudative tuberculosis. Patients with elevated 17-ketosteroids in the urine exhibited well-localized, fibrotic or nodular tuberculosis. There were exceptions to this general relationship suggesting that factors other than severity of disease were influencing adrenocortical function.

It was observed that 17-ketosteroid excretion appeared to be consistently related to the emotional state of the patient (see case of male physician above). Patients with very low levels of excretion were overtly depressed, apathetic, and withdrawn. Patients with normal values were reasonably comfortable in their adjustment. Those with above normal output were tense, conflict-ridden, and exhibited the well-known clinical signs of anxiety, such as restlessness, irritability, insomnia, tachycardia, labile blood pressure and palmar sweating.

Rapid and profound changes in 17-ketosteroid excretion were observed to accompany changes in emotional states resulting from acute or chronic stress situations arising during the course of hospitalization. These alterations in adrenocortical function persisted for the duration of the emotional response.

Despite standard antimicrobial therapy, distinct trends in the course of the disease were evident. Patients whose 17-ketosteroid output remained stationary near the normal level showed satisfactory improvement in their disease as did those whose level of output was changing toward normal from above or below. In contrast, patients with a stationary excretion level at some distance above or below normal improved slowly or not at all. The degree of improvement was related to the proximity of the excretion to the normal level. The patients whose disease became worse and those who died exhibited progressive depression and low or declining excretion.

Comment.—The 17-ketosteroid excretion observed in these cases indicating significant alteration of adrenocortical activity in tuberculosis is in agreement with the findings of others (59-63). The fact that alterations in 17-ketosteroid excretion parallel changes in the course of tuberculosis suggests that

endogenous adrenocortical hormones influence resistance to tuberculosis. From these observations it is suggested that adrenocortical activity plays a role in resistance to tuberculosis and that the effects of life stress upon the course of tuberculosis, in part, may be mediated via the adrenal gland.

FORMULATION

In daily living, the relationship of tribal man to his environment is constantly influenced by stimuli of widely varying origin, character, and significance. Alterations in behavior occur only in response to certain of these stimuli. Further, the degree to which afferent impulses evoked by a given stimulus are consciously perceived and evaluated is variable and may or may not be relevant to the ensuing reaction. The character and significance of such changes in behavior as do occur will be largely determined by the stimulus situation, the individual's biologic endowment, and his past experience. Viewed from a biologic perspective these modifications in behavior appear to be adaptive and protective.

In response to life stress, patterns of adaptive and protective behavior may be relatively free from anxiety. These include phobic, amnesic, compulsive, obsessive, hypochondriacal, and conversion hysterical reactions. Closely allied are the processes of repression and rationalization. Although these reactions may be due directly to frustration, deprivation, and symbols of danger, they often represent the techniques utilized for attempting to re-establish homeostasis after the threat has been acknowledged and anxiety and tension have occurred. Although these methods for dealing with problems may be more or less successful, they seriously impair performance and restrict capacities for flexibility and maturity. In addition, these patterns of behavior may themselves contribute to the genesis of anxiety.

The occurrence of anxiety as the only emotion present has seldom been encountered in these psychophysiologic studies. Rather, the response of which anxiety is a part is composed of a medley of feeling states of various combinations and intensities: guilt, anger, hostility, resentment, humiliation, euphoria,

depression, etc. Functional alterations of the biochemical and physiologic systems of the body invariably accompany these emotional states and are mediated by neurohumeral mechanisms. Important to the specificity and character of integration of these psychophysiologic components of behavior is the way in which the individual perceives his relationship to a given situation and what if anything he does or feels like doing about it. The effectiveness of these adaptive and protective patterns of behavior depends on their pertinence to the stimulus, their magnitude and duration. The mobilization of bodily resources when appropriate in context may facilitate the resolution of danger and conflict at little cost to the individual. When inappropriate, these functional alterations in homeostatic mechanisms become sustained and productive of discomfort and tissue destruction. Not only do they fail to achieve their purpose, but actually are responsible for the genesis of additional danger and threat to security.

A concept long recognized by students of human behavior is that early conditioning experiences play an important role in determining the character of an individual's behavior and adjustment in later life. It has been emphasized further that these early experiences are significant factors in many psychiatric illnesses, often through the activation of anxiety. More recently in investigations of the natural history of a host of "psychosomatic disorders" (27), much speculative emphasis has been placed on the importance of these early life situations to the evolution of specific patterns of psychophysiologic responses which may be productive of selective organ dysfunction and symptoms in later life. The observations on infants reported here document the origin of some of the psychophysiologic reactions which may contribute to the evolution of specific and repetitive anxiety reactions and disease.

Considered in social context, man's concept of himself and his conformance with what is expected of him results in large part from the cultural milieu in which he lives. The evolution of attitudes, values, aspirations, and techniques for achieving goals which approximate the tribal norms is essen-

tial to homeostasis, productivity and satisfaction. The success of this process of cultural conditioning depends in part on the nature of the individual, the nature of social pressures and the effectiveness of dealing with them. Stable civilizations provide a milieu in which the individual can usually define his status with relative ease. In such a way of life the possibilities for culture conflict are minimized and the techniques for resolving tensions are reasonably effective. By contrast, in societies undergoing rapid change, as in the United States the individual often experiences considerable difficulty in finding his place and making accurate discriminations concerning what is and what is not dangerous. The possibilities for culture conflict abound and the techniques for dealing with ensuing difficulties become attenuated. As a further consequence the individual's knowledge concerning the availability and applicability of these methods is often faulty or incomplete. Therefore, anxiety, discomfort, tissue damage, and impairment of performance, which occur as by-products of attempts at adaptation, become inextricably linked to cultural conflict.

SUMMARY

Inherent in man's biologic endowment is the need for homeostasis and the equipment for its maintenance. Assaults upon and threats to his physical and emotional integrity which upset this homeostasis provoke adaptive reactions intended to restore the equilibrium within the internal milieu of the body, and between the body's internal and external environment. Such reactions to life stress usually are manifested as alterations in behavior which may vary widely in degree, content, duration, and effectiveness. When sustained these reactions may be productive of discomfort and impairment of tissue integrity. Many of the illnesses experienced by man, then, may occur in large part as a by-product of his attempts at adaptation.

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PRELIMINARY CLINICAL REPORTS

CHLORPROMAZINE IN THE TREATMENT OF MENTAL ILLNESS: A STUDY OF 750 PATIENTS

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Chlorpromazine hydrochloride [10-(γ -dimethylaminopropyl)-2-chlorophenothiazine hydrochloride] has been used as the sole form of treatment in 750 patients at Manhattan State Hospital. Five hundred seventy-one were diagnosed as dementia praecox, while the others were distributed through 14 different diagnostic groups. Four hundred ninety-four patients had been hospitalized from 3-10 years. Electroconvulsive therapy, insulin coma treatment, and lobotomy alone or in combination, were the previous unsuccessful treatments administered to 493 patients.

The duration of chlorpromazine treatment varied from 1-5 months, with 444 patients receiving the drug from 2-5 months. The dose ranged from 50 mg. to 900 mg. daily, with 327 patients receiving 300 mg. daily. Both oral and intramuscular routes were used; in the latter case hyaluronidase was added to facilitate absorption and prevent abscess formation.

Results.—48 patients have been discharged, and 5 are ready for discharge; 48 patients were markedly improved; 475 improved; 174 patients showed no change. At the present time, electroconvulsive treatment has been discontinued on the female wards, and is rarely used in the male services. Insulin coma treatment is only occasionally used. Large numbers of previously detached, seclusive, aggressive, and combative patients now attend occupational and recreational therapy, take part in social activities, and have ground privileges. Physical restraint has been decreased 74% and accidents by

75% in the female wards. This change has been slower on the male services where patients have been under treatment for a shorter time.

The most important side effects noted were Parkinson syndrome (32 patients), skin rash (20 patients), jaundice (13 patients), hypotension (13 patients), and convulsive seizures (11 patients). There were no blood dyscrasias (i.e. agranulocytosis). The incidence of all side effects increased with the height of the dose. Parkinson symptoms appeared as the duration of treatment was prolonged. However, promethazine hydrochloride (50-150 mg. daily) decreased and abolished these symptoms during the concomitant administration of chlorpromazine.

The most effective dose of chlorpromazine was 300 mg. daily. The optimum duration of treatment for acutely ill patients appears to be 2 months; this, however, may vary from patient to patient. Chronic patients will undoubtedly have to be treated for longer periods.

The effects of chlorpromazine medication vary inversely with the duration of hospitalization. Nevertheless, it was still possible to discharge 17 patients, ill from 5 to 10 years, 3 of whom had been unsuccessfully treated previously with electroshock insulin coma, and lobotomy.

Conclusion.—Chlorpromazine hydrochloride has effectively broadened the scope of treatment in psychiatry. At present, the questions of relapse rates, maintenance dose, and methods of controlling side effects are under study.

COMMENT

BLUE CROSS, BLUE SHIELD, AND THE BLUES

The most successful insurance enterprise in the world is probably Blue Cross. And its medical-service counterpart, Blue Shield, does not lag far behind. Nearly everyone touched by Blue Cross has been helped. But not quite everyone. One large group of patients and one small group of physicians can hardly find standing room beneath the Blue Cross umbrella. The excluded group is made of psychiatrists and their patients.

In all fields, except psychiatry, Blue Cross pays for about 75% of the average subscriber's hospital bill. Blue Shield pays for about 45% of the average subscriber's physician's bill. In psychiatry, payments made by these agencies are trifling. In general, Blue Cross and Blue Shield discriminate against the psychiatric patient. Many policies unequivocally exclude psychiatric cases. Others allow lesser benefits for psychiatric conditions than for medical or surgical disorders. Some policies require evidence of "organic" disease; some exclude treatment in "special" wards; many limit benefits to "general" hospitals. Some exclude disorders due to alcohol or drugs. Many policies do not cover care of "self-inflicted injuries"; accordingly, if a patient cuts his throat in a depressive episode, the surgical repair is excluded from the Blue Cross coverage. There are policies which pay for lung surgery but not brain surgery, or which do not cover psychoneuroses once that diagnosis is established. There is even one policy which pays for nervous disorders but not for mental disorders. More generous is the policy which pays for "all self-inflicted injuries . . . except those which are intentional." One curious policy reimburses for self-inflicted injuries unless due to a psychiatric condition.

The conscious reasons for excluding psychoneuroses and psychoses are given as follows: (1) emotional illness is so common that it would bankrupt the Plan; (2) there is no sharp line between illness and oddity; for instance, no exact frontier between laziness

and neurasthenia, homosexuality and psychoneurosis with sexual regression, alcoholism as sickness and alcoholism as character defect, and so on; (3) the volitional and motivational elements are too strong to make psychoneurosis an insurable risk; (4) there is no actuarial basis on which the incidence of psychoneurosis can be calculated, and therefore there is no way of determining how much extra premium to charge; and (5) psychiatrists won't accept the 3, 4, and 5 dollar fees which make it possible for Blue Shield to meet the bills of other specialists.

Behind these conscious reasons lies, one suspects, the feeling that psychoneurosis is a voluntary, self-induced, basically unreal disability which reflects weakness of character. One Blue Cross official (in what the Washington journalists call a "non-attributable briefing") said: "We are not going to use subscribers' money to pay for rest cures, to buy sobering-up vacations for drunks, or to coddle a hypochondriac while he enjoys himself in a hospital bed, at our expense."

What happened to our educational devices? We thought that the public had long since been "educated out" of this philosophy. But there you have it.

As a matter of fact, some kind friend should educate the Blue Cross officials to the fact that they are kidding themselves. Someone ought to tell them that they are paying for hypochondriacs and other neurotics. Bennett and his co-workers,¹ for instance, reported that in 10% of a block of general hospital cases, Blue Cross paid out \$5,000 for unnecessary laboratory work in the course of treating emotional illness. There had been an endless round of expensive tests undertaken in the hope of somehow finding some "organic" diagnosis that would enable the patient to get something out of the insurance he had already paid for. If

¹ Bennett, A. E., Hargrove, E. A., and Engle, Beatrice. *Psychiatric Treatment in General Hospitals*. J. A. M. A., 147: 1019, Nov. 10, 1951.

psychiatric services had been covered, there would have been encouragement for earlier psychiatric consultation and swifter psychiatric treatment—thus saving the costs of futile nonpsychiatric care and “negative” laboratory and X-ray studies. And incidentally, the companies would sell more policies.

The one still unanswerable difficulty—as it applies to Blue Shield at least—is the matter of the therapist’s fee. The economic structure of Blue Shield apparently cannot support per-visit fees of more than 4 or 5 dollars. Cardiologists, pediatricians, orthopedists, and allergists seem willing to accept such fees. Psychiatrists do not accept them, because the psychiatrist spends so much more time per patient-contact than does any other medical specialist.

This faces our specialty with a formidable challenge. Voluntary health insurance is here to stay, and if psychiatry wants to be part of medical practice, we ought to be part of this enterprise. What kind of compromise can we reach with respect to fees? Perhaps we could analogize a psychiatric disorder to a surgical one. At least psychotherapy has

been described as surgery without an anesthetic. If Blue Shield can pay a surgeon \$125 or \$175 for an hour’s work in the operating room, why cannot it pay a psychiatrist \$150 for ten hours’ work at the bedside or in the interview room?

We in psychiatry have put vast effort into the campaign to convince the public that a psychiatric diagnosis is not a stigma, that it does not essentially differ from a medical or surgical diagnosis. But the patient finds that his Blue Cross premiums are often wasted if he suffers from an emotional disorder, whereas he can be reimbursed for a diagnosis in any other branch of medicine.

Blue Cross and Blue Shield officials are doing very well without us. On their own they will make no move to change the present practice.

The next move is ours.

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Note: A more detailed study of this problem will be found in the October 1954 report of the *Ad Hoc* Committee on the Economic Aspects of Psychiatry. A copy of this report may be procured from the Medical Director’s office so long as the present supply lasts.

HISTORICAL NOTE

THE ORIGIN AND EARLY HISTORY OF ELECTROTHERAPY AND ELECTROSHOCK

American psychiatric literature is surprisingly lacking in any discussion or mention of electrotherapy, a widely discussed topic in every major European textbook since 1850. Not before 1940 is electroshock mentioned and its invention is ascribed to the Italian Ugo Cerletti(1). A check of the original manuscript shows that it is a 2-page report from the clinic of which Cerletti is the director. The experiment was done by Dr. L. Bini who is introduced as an expert electro-technician. The experiment concerns the success of a high voltage shock administered to an epileptic male who was considerably improved after receiving this treatment. This experiment was one of the many conducted by this clinic mainly devoted to epilepsy(2) which was a popular field for study in Middle European neurology; and studies such as "Experimental Convulsions"(3) and "Convulsions Resulting from Electric Treatment"(4) were common topics as far back as 1880.

However, one can trace such electrotherapy back to 1740 when, shortly after electricity had been experimentally isolated, its application for medical purposes started long before the idea matured that it would be such an important technical factor. Beginning in 1744, the *Histoire de L'Academie Royal des Sciences* of France(5) brought out a report on "Electricity and Medicine" every second year. There are "guerisons" (cures) reported from all over Europe; from the Italian "miracle" priest Abbe Nollet, from the Swiss Louis J. Jallabert, from the Dutchman Leyde, and from a number of others. Among the cures reported, a majority were neurological and mental cases of paralysis and epilepsy. In the report of 1755, pages 9 to 11, a Frenchman, Dr. J.B. Le Roy reports in detail his cure of what today may be called a case of hysterical blindness(5). After the patient received his first "commotion" (shock), he reacted with convulsions of the eyes and he saw rays of light for the first time. When

he received 3 shocks, the third somewhat stronger than the others, he screamed and fainted, and as a result of this treatment he began to regain his eyesight. There is no doubt that we are presented here with an actual electroshock treatment and probably the first one. In 1801, the German electrotherapist Friedrich L. Augustin(6) reports an almost identical case. With the beginning of the nineteenth century, however, electrotherapy fell into disuse. The reason seems to be that the scientific mind was not satisfied with the inexact application of an unmeasured amount of electricity, for we know that the first 3 decades of the nineteenth century was the period when the mechanical and technical knowledge of the physics and chemistry of electricity was developed.

During that same period the problems of shock as a therapeutic means was a concern of the first psychiatrists who desired to find a purely psychological therapeutic technique to aid mental ailments. S. Kornfeld mentions a number of such men in his short *History of Psychiatry*(7). Among those mentioned is the amazing F. C. G. Scheidemann who, in 1787, wrote the first textbook of psychosomatic medicine(8). In it he has 2 chapters on "fright" and "scare" as a means of cure. Here, in detail, he enumerates a number of illnesses in which he believes shock may be of help. These range from hiccoughs and convulsive laughter to indigestion, menstrual bleeding, hysterical paralysis, epileptic attacks, and mass neurosis.

During the 1830's electrotherapy came into use again as a therapeutic agent with nervous and mental diseases; however, it was in a form other than the undifferentiated use it had in the past century. There was a differentiation between galvanic and feradic electricity, the various strengths, long- and short-term application, etc. After 3 decades the development of this new scientific electrotherapy had matured to the point that an Aus-

trian-Hungarian neurologist Moriz Benedikt had enough material to write 2 larger works(9, 10) giving specific prescriptions for all known and somatically fixed neuro- and psychopathology. The Bavarian medical writer Johan B. Ullersperger(11) received an academy price for a synoptic description of electrotherapy. The Frenchman G. B. C. Duchenne, who is sometimes called the father of modern electrotherapy and who wrote an entire set of works on the various phases of this subject(12), demanded that no sincere neurologist could practice without using electrotherapy. The most important contributor to this entire development, however, seems to be the German psychiatrist Rudolf Arndt who, in a 130-page study(13), did the most to unveil the psychological and organic background of the role and influence of electricity with regard to neuro- and psychopathology. The most advanced of our present electroshock therapists(14) must confess that they know only about the effects of their methods and nothing about the cause and the other determining factors regarding the influence of electricity upon our body and its nervous system in general and upon mental abnormalities in particular.

Even if the theoretical aspect and organic knowledge of Rudolf Arndt is outmoded, his approach to the study of electricity in its relationship to psychiatry seems to contain the method the present shock therapists should use to gain a sound understanding of what

makes electricity a good (or bad) therapeutic agent for psychiatric disorders.

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NEWS AND NOTES

NEW COURSE IN RELATIONSHIP OF PSYCHIATRY AND LAW.—A 3-year program for teaching law students the relationship of psychiatry to modern legal problems will be developed by the University of Pennsylvania Law School under an \$89,640 federal grant, according to an announcement by Dean Jefferson B. Fordham.

The project will be conducted within the framework of the University's existing Institute of Legal Research; however, general responsibility for its progress will be vested in a supervisory committee, Louis B. Schwartz, professor of law, chairman.

In charge of the project's day-to-day operation will be 2 co-directors: a professor of law, who will devote full time to the work, and a psychiatrist, who will give half his time to the venture.

Attention will be focused on such topics as criminal prosecution and defense, commitment of the mentally ill, divorce, and legal capacity to contract, marry, and make a will.

KAREN HORNEY CLINIC.—On May 6, 1955, the Karen Horney Clinic, a nonprofit, free, and low-cost psychiatric clinic, was opened at 115 East 31st Street, New York City. It will be operated by the Karen Horney Foundation in association with the American Institute for Psychoanalysis, which will provide the medical staff and supervise the treatment program.

Dr. Horney was a founder of the American Institute for Psychoanalysis and served as its dean until her death in 1952.

The clinic will accept referrals from private and public agencies. Individuals may also apply directly. For further information call Milton Berger, M. D., BU-2297.

REHABILITATION OF THE DEAF.—The Office of Vocational Rehabilitation of the U. S. Department of Health, Education, and Welfare has approved a grant of \$27,800 to the New York State Psychiatric Institute for establishing a mental hygiene clinic for deaf adolescents and adults. The Institute will

operate in 3 important mental health areas for deaf people—research, service, and training of others to serve as mental hygiene workers for the deaf. Dr. Franz Kallman, Columbia University, and a member of the Institute staff, will direct this new rehabilitation service.

AMERICAN EEG SOCIETY MEETING.—The ninth annual meeting of the American Electroencephalographic Society will take place at the Palmer House, Chicago, Illinois, June 10, 11, and 12, immediately preceding the annual meeting of the American Neurological Association. The scientific sessions will be held on Friday, June 10, at 2:00 p.m. and 8:00 p.m., and on Saturday, June 11, at 2:00 p.m.

There will be 2 symposia: one, on micro-electrodes on Saturday, June 11, from 1:30 a.m. to 12:00 noon, under the chairmanship of Dr. Herbert H. Jasper; another, on clinical EEG interpretation (head injuries), Sunday morning, June 12, from 9:30 until noon, under the chairmanship of Dr. Frederic A. Gibbs.

The annual banquet will take place Saturday, June 11, at 7:30 p.m. Business sessions will be held Friday, June 10, 4:30 to 6:30 p.m. and 10:30 p.m.

DR. LEWIS WOLBERG HONORED.—On Friday, April 15, 1955, at the Savoy-Plaza Hotel in New York City, a testimonial dinner celebrating the tenth anniversary of the Postgraduate Center for Psychotherapy was given to Dr. Lewis Wolberg by the board of trustees and professional staff. Dr. Wolberg, as founder of the Center, was commended for having supported the principle of eclecticism in the teaching program, wherein the contributions of the various schools of psychiatric thinking are studied and utilized.

CROWNSVILLE STATE HOSPITAL.—This hospital, located at Crownsville, Maryland, is devoted exclusively to the care of Negro patients and serves the entire State of Maryland. Its professional staff represents all

disciplines and includes white and colored professional workers. The hospital has been approved by the Council on Medical Education and Hospitals and the American Board of Psychiatry and Neurology for one year of residency training in psychiatry and affords an unusual opportunity to become acquainted with the problems of a particular group in a state hospital setting. It is one of the few hospitals of its sort approved for training.

For further information concerning this training opportunity, write to Leon Eisenberg, M.D., Director of Psychiatric Education, Crownsville State Hospital, Crownsville, Md.

NATIONAL COUNCIL ON FAMILY RELATIONS.—The next annual meeting will be held August 25-27, 1955, at the University of Minnesota, Minneapolis, Minn. Theme: The Family Tomorrow, with Emphasis on the International Aspects of Family Life.

Five general sessions are planned on the following subjects: (1) Keynote address by an internationally known figure, Mrs. Eugenia Anderson, former United States Ambassador to Denmark; (2) highlights of family life in other countries; (3) family counseling; (4) family protective services around the world; (5) health and the family. Section meetings will be related to the general sessions. Two or three papers will be presented at each section meeting with ample provision for discussion.

Advance registration can be made directly to Mr. James Schroeder, Centennial Hall, The University of Minnesota, Minneapolis 14, Minn. Total charge for room, Wednesday through Saturday night, 12 dollars per adult; room charge per night, 3 dollars; meals at moderate cost. Inquiries on local matters should be directed to Mr. Robert J. Swan, Director of Guidance, Alexander Ramsey Junior-Senior High School, St. Paul 13, Minn. Inquiries of general National Council matters should be directed to Mr. Armond D. Willis, Executive Secretary, National Council on Family Relations, 5757 South Drexel Avenue, Chicago 37, Ill.

SPRINGFIELD (MARYLAND) STATE HOSPITAL.—The Department of Psychology, Springfield State Hospital, announces that

the third annual Springfield Lecture has been renamed the Virginia Beyer Lecture in honor of the late Virginia Beyer, M.D., former clinical director of Springfield State Hospital. Dr. Beyer came to Springfield in August 1925 and died in September 1954. When the Department of Psychology was conceived in 1950, Dr. Beyer readily gave of her time, collaboration, and influence to make the department what it is today, a total force of 14 persons.

The first Virginia Beyer Lecturer is Stuart C. Miller, M.D., of the Austen Riggs Center, Stockbridge, Massachusetts. The dates are June 24 and 25; the topic, "Contemporary Psychoanalytic Ego Psychology." Registration fee is 10 dollars. For further information write to Dr. Michael H. P. Finn, Chief Psychologist, Springfield State Hospital, Sykesville, Maryland.

EAST BAY (CALIFORNIA) PSYCHIATRIC ASSOCIATION.—The officers of this society for the year 1955 are as follows: Dr. Douglas Kelley, president; Dr. William Sheehy, president-elect; Dr. James Davidson, secretary; Dr. Clement Juul, treasurer. Drs. Lewis McKeever and Jessie Enslin have been elected as councillors.

NEW RATES IN PUBLIC HEALTH SERVICE TRAINEESHIPS.—The U. S. Department of Health, Education, and Welfare announces that the support provided by the Public Health Service traineeships awarded each year by the National Institute of Mental Health has been increased. The new rates authorized by the National Advisory Mental Health Council are as follows: Level 1, \$1,800; level 2, \$2,000; level 3, \$2,400; level 4, \$2,800; level 5, \$3,400; level 6, \$4,000.

For traineeships in psychiatry: first year, level 3: \$2,400; second year, level 4: \$2,800; third year, level 5: \$3,400. For postgraduate psychiatric training beyond the third year, level 6: \$4,000.

A list of institutions authorized to administer Public Health Service traineeships is available on request from the Training and Standards Branch, National Institute of Mental Health, Bethesda 14, Maryland.

TESTIMONIAL TO KNUD H. KRABBE.—Combined numbers One and Two of Volume

30 of the *Acta Psychiatrica et Neurologica Scandinavica*, published in March 1955 and dedicated to the eminent neurologist by his friends and student, contains 37 articles by his colleagues, together with a full bibliography of publications by the chief, prepared with the assistance of the staff of the neurological department of the Municipal Hospital, Copenhagen. An excellent photograph of Dr. Krabbe prefaces the volume.

THE HEBREW MEDICAL JOURNAL.—This journal is a bilingual, semi-annual publica-

tion, now in its twenty-seventh year. A distinguishing feature is the part it is playing in the revival of the Hebrew language as a living tongue for scientific communication.

Volume 2, 1954, contains timely medical and also historical articles. Of special interest is a collection of short articles on the famed Jewish physician and philosopher, Maimonides, in commemoration of the 750th anniversary of his death.

The editor of the *Hebrew Medical Journal* is Moses Einhorn, M. D., and the office of publication is 983 Park Avenue, New York 28, N. Y.

BOOK REVIEWS

PSYCHIATRIC TREATMENT. Research Publications, Association for Research in Nervous and Mental Disease, Vol. XXXI. By *S. Bernard Wortis, et al.* (Baltimore: Williams & Wilkins, 1953. Price: \$9.00.)

Thirty-three papers plus 8 summaries and the introduction by the Association's President, S. Bernard Wortis, all read at the meeting of the Association for Research in Nervous and Mental Disease meeting in December 1951, comprise the material of this volume. The first 17 papers deal with individual and group psychotherapy; the next 9 with biological, electrical, and pharmacological treatments; the last 8 evaluate neurosurgical treatments.

These articles are all of high quality and the book should be read by every person who wishes to keep up to date on therapy. It may be remarked, however, that in the short interval between the time the papers were read and the time this review is written, 2 new drugs, chlorpromazine and reserpine, have markedly affected physiological treatment and raise some question about many of the conclusions in the second and third parts of the book (Sections XVIII to XXXIII).

With so many excellent papers, it is impossible to review them all; and the reviewer has arbitrarily picked for discussion 3 papers that appeal to him most.

The first paper, by John C. Whitehorn, is entitled "Therapeutic Goals and Their Significance for Therapeutic Strategy." Whitehorn feels that one intervenes with therapy for generally one of 3 objectives (sometimes all 3 at once): "(1) to save from death, (2) to relieve from distress, and (3) to overcome disability." He points out a number of different approaches. The therapist may, by surgery, electricity or drugs, wound the disabling part of the personality which has caused the patient's self-disablement, in the hope that the mutilated whole will function better than before. "Social improvement" is considered evidence of successful therapy.

A second group of psychiatrists consider that disturbances of interpersonal relationships constitute the basic psychopathology, and the ordinary symptoms are but manifestations of these morbid interpersonal attitudes—to be viewed as "the disease."

Another point concerns anxiety. Some therapists wish to relieve anxiety, in line with the general medical goal of relieving distress. Others feel that freeing the patient from anxiety takes away the drive necessary to help him achieve real improvement.

This scholarly, stimulating chapter discusses many other viewpoints, including the recent argument in psychoanalytic circles concerning Alexander's formulations about psychoanalytic therapy, which the author considers "not merely a dispute

about method but also a difference in therapeutic goals."

Franz Alexander's "brief" chapter, "Principles and Techniques of Brief Psychotherapeutic Procedures," presents considerable controversial material. Alexander finds that the long drawn-out psychotherapies are really supportive even if they start as uncovering procedures, and that many brief psychotherapies, begun as supportive, become uncovering as the patient's anxiety subsides. Defining 3 basic functions of the ego, he lists 5 procedures commonly used in supportive therapy. He also objects to "a widely-held erroneous view, namely, that briefer psychotherapeutic methods require less technical and theoretical preparation" than does psychoanalysis.

A very interesting chapter, "Long Term Psychotherapy," by Appel, Lhamon, Myers, and Harvey, gives a most careful and detailed analysis of statistics. The most important conclusions deal with the results of psychotherapy in psychoneuroses and in schizophrenia; and point out that while there may be many errors in the available statistics, the best possible analysis shows essential "similarity of results" by various types of psychotherapy. An excellent discussion of possible interpretations of such figures follows. The authors conclude: "No one type of approach is best for all. Although one notes a regrettable tendency among many psychiatrists to adopt a stereotyped therapy, treatment to be helpful should be individualized in terms of the individual patient."

Lack of space prevents a discussion of the many other interesting articles in this book. It should be a "must" reading for everyone interested in psychiatry.

K. M. B.

BARN, SERIEN, SAMHAELLE. (Children, Comics, Society). By *Nils Bejerot.* (Stockholm: F. I. B. Publishers, 1954.)

While there still was a tendency in this country to regard the comics problem as a rather indifferent side issue, which only tended to be blown up into undue proportions by Dr. Fredric Wertham and his colleagues at the Lafargue Clinic, the same problem was already getting serious attention in other countries across the Atlantic. Both in the daily press and in psychological journals in Sweden, Denmark, Holland, and England, the problem was being recognized as a potentially very serious one. The author of the present book, Nils Bejerot, a psychologist in the Child Welfare Department of the City of Stockholm, finally went in for extensive research as to the nature and effects of crime and horror comics, and has come up with some very interesting findings.

While he has read and quotes from Wertham's

book, *Seduction of the Innocent*, which appeared only a short time before the publication of his own book, it is evident that he has done comprehensive independent research of his own and that the conclusions at which he arrived are remarkably similar to those of Wertham. While it would seem clear enough that the veritable flood of crime comics, which have been released in Sweden to nearly the same extent as in this country, must necessarily have some effect by the sheer repetition of their themes, Bejerot has substantiated this by statistics as well as with case histories.

What seems particularly impressive about this book is that the author has presented his findings in a highly condensed form which aids the reader in seeing the data involved in clear and sharp relief. It seems worthwhile to quote some of his statistics by which he attempts to show the magnitude of the influences at work. According to his figures, Swedish children are subjected to the following fantastic numbers of pictures of crime and violence during a single year (p. 95):

War-like activities	5 billion
Murder and killing.....	4 billion
Attempted murder and threat of murder.....	13 billion
Physical violence	7 billion
Cruelty and sadism.....	3 billion
Other acts of personal violence	17 billion
Other crimes	15 billion
Show of weapons.....	26 billion
Threat with weapons.....	7 billion
Shooting incidents	6 billion

This amounts to approximately 100 billion acts of violence in the 167 billion pictures which represent a year's edition of all the crime comic books released in Sweden.

In his analysis the author points to roughly the same attitudes and ideologies that Wertham uncovers in his analysis of the same material. His juxtaposition of commonly accepted productive and social human attitudes with the attitudes shown and propagated in the comic books deserves to be quoted. In a brief paragraph entitled "Stones Instead of Bread," the author says: "Instead of adventure and action: violence, crime, brutality, sadism, torture, war and death. Instead of imagination: fantasies of horror and fright. Instead of heroes: savage and maniacal muscle-monsters out to destroy their enemies in any way or fashion whatsoever. Instead of heroines: ruthless jungle Amazons, silly, vacillating and insipid sweater girls, or depraved nightclub queens. Instead of love: egotism, envy, intrigue and obsessive sexuality. Instead of friendship: distrust, envy, hatred and defamation. Instead of understanding between peoples and nations: race discrimination, master race ideologies, spying, blockades, hostility and war. Instead of 'humor': stupid platitudes or sadistic catastrophes and misfortunes. Instead of knowledge and education: distortions and pseudoscientific absurdities and ridicule of civilization and science. Instead of a sound view of life: a power philosophy,

an ideology of 'might makes right' and 'an eye for an eye and a tooth for a tooth'."

It is of course impossible that the propaganda of sadism and pathological behavior should remain without results. Wertham has cited various instances in which the reading of comic books could be directly traced in the behavior of children, who are described as criminals after they have practiced what they have learned. Bejerot cites numerous instances of the same kind. One 9-year-old child tied his 4-year-old playmate to a tree, surrounded him with twigs and set fire to them. The child then told how he had gotten the idea from a comic book. Another child was electrocuted by a power line in his attempt to fly like Superman. In another instance, three 13-year old boys in Helsingborg hanged a 9-year-old from a tree and then beat him so badly that he needed medical treatment.

There are many stories of this kind cited in the book. There is also a brief excerpt from a novel submitted by a 16-year old, whose subject matter was borrowed wholesale from crime comics and shows a brutality that would seem incredible outside a clinical case-history or a murder report. It is surely not purely coincidental that the mass import of American crime comics into other countries would seem to lead to the same kind of consequences there that Wertham has pointed to in his writings. Swedish and Danish psychologists and educators have called attention to the problem created in their countries as far back as 1949, without knowledge of the Wertham research. For various reasons, the evidence seems to pile up that despite all the current evasions and obfuscations of the problem by interested persons, 2 and 2 still add up to 4, and you cannot initiate a destructive propaganda campaign (which is what the comic-book flood actually is) without getting corresponding results. Every copy boy in an advertising agency knows as much. But the educated, the learned, and the therefore supposedly more responsible in all the nations involved, still seem somewhat hard to convince. It could easily become monotonous to cite further examples adduced by the author both from his own country and from Denmark and England. But it seems as though all the necessary research, painstaking, conscientious, and well-documented, is already in. Fortunately public opinion—and in consequence also legal endeavor—is being mobilized in Sweden as well as in England, where the criminal propaganda of the comic-book variety is sensibly being regarded in the bills under consideration as a criminal offense.

An excerpt from an address by a Danish educator, Søren Christensen, is cited by the author: "If you who are educators maintain that these comic books are educationally, humanly or morally defensible and even constructive, then you should as soon as possible acquire them for your school libraries, since you thereby would save the children the expenditure and, in addition, would gain considerable visual material for an effective education in civilized living. If, however, you share my opinion that these books are the worst and most deliberate traffic in idiocy and psychic poisoning that any civi-

lization has ever brought forth, then you must also accept the consequences of this insight. You must ask yourselves: 'Do my pupils not deserve a better fate than to become co-citizens in the kind of world that abounds in bandits, gun-shooting gangsters, spies, superhuman white people and sub-human colored people—a world in which bestiality, brutality, sex craze, gold-digging, race hatred and stupidity reign supreme?'

There are very good illustrations from comic books which form an important part of the documentation. There are comic books with English text and American and American-style comics with Swedish text. The author pays particular attention to the instillation of race hatred. On page 98 he reproduces the heads of 21 comic-book heroes taken from as many different comic books and drawn by different artists. He comments that the heroes are all alike—standardized young men, strong, athletically built, with rectangular faces and regular features, a straight nose and square chin. They are fine examples, he says, of the highly appreciated Aryan race. The villains, on the other hand, are unattractive, repulsive, often deformed and with crooked noses. Bejerot points to the monotony and uniformity of the plots which make it irrelevant to classify comics as Westerns, Superman, space, etc. "The action may take place anywhere, from an obscure bedroom to a mysterious universe. The characters are always just exactly the same, wherever they may happen to be."

The book has a good bibliography and includes an account of the history of comic books. It is written in a sober, critical, and thoroughly scientific manner. Only in the very last sentence does the author address the publishers of objectionable crime comic books. And even here he does not use his own words, but quotes the famous Swedish author Strindberg: "You have no other legitimate demands than to be abolished." This is an excellent book which deserves a wide audience among psychiatrists, psychologists, and educators.

SIGFRID VON KOCH, PH. D.,
New York City.

ADRENAL CORTEX. Transactions of the Fifth Conference. Edited by Elaine P. Ralli. (New York: Josiah Macy, Jr. Foundation, 1954. Price: \$3.75.)

The well-known conferences of the Josiah Macy, Jr. Foundation deal with special topics in the medical sciences. Each lasts 2 days and occurs annually for a five-year period. This is the fifth conference on the adrenal cortex and was participated in by 22 distinguished investigators. The form of publication of the Macy conferences is of special interest since the formal presentation of topics is brief and is followed and often interrupted by lively discussion.

The present volume considers 3 main topics. Dr. H. L. Mason of the Mayo Clinic begins the symposium with a consideration of "the salt and water factor of the adrenal cortex." The volume was published a year after the conference, and since this

particular topic has moved with great rapidity in the past 2 years, considerable advances have been made recently. Prior to the conference, Dr. Reichstein and his associates had announced the isolation of "electrocortin." Dr. Mason reviews some of this work and then describes methods in use in his laboratory for isolating the substance by chromatography. More recently the structure of electrocortin has been determined by Reichstein and collaborators and the name "aldosterone" adopted for it. The substance is an exceedingly potent regulator of electrolyte metabolism.

A very significant contribution is presented by Dr. Ralph I. Dorfman of the Worcester Foundation for Experimental Biology on "the metabolism of adrenal steroids." Dorfman and his collaborators have developed a technique for identifying the secretory product of the adrenal cortex *in vivo* in man by analysis of urinary steroids. This ingenious approach has made it possible to obtain new information about adrenal function in various endocrine disorders. Dorfman's presentation especially is applied to hyperfunction of the adrenal in cases of adrenal carcinoma, the adrenogenital syndrome, and Cushing's disease. His method of analysis has been published elsewhere within the past year but the presentation and discussion in the Macy conference is especially readable and illuminating. The approach has far-reaching implications for the practice of endocrinology.

The volume concludes with a paper by Frank G. Young, professor of biochemistry at Cambridge University, on the subject of "ACTH—a single substance or a mixture of hormones." By chromatographic procedures, Young and his associates have isolated different polypeptide fractions from crude pituitary preparations, one of which is primarily concerned with the regulation of adrenal weight while the other is primarily involved in adrenal ascorbic acid depletion. The nature of various active polypeptide fractions varying in effective adrenal stimulating properties is discussed by the conference participants.

HUDSON HOAGLAND,
Shrewsbury, Mass.

STEREOENCEPHALOTOMY (THALAMOTOMY AND RELATED PROCEDURES), PART I. METHODS AND STEREOTAXIC ATLAS OF THE HUMAN BRAIN. By E. A. Spiegel and H. T. Wycis. (New York: Grune & Stratton, 1952. Price: \$8.00.)

In an era when selective procedures are being developed in the field of psychosurgery, this monograph is of considerable importance. Working painstakingly with a newly devised stereotaxic instrument for application to the human individual, the authors have been able to place lesions in the deeper structures of the brain within 1.5 mm. of the target in almost all instances. At the same time, they have been able to fix the location roentgenographically by means of injection of a few drops of contrast material. The 3 planes intersect at the posterior commissure as determined by pneumoencephalography. The vertical plane passes through

this spot and the pontomedullary groove. The horizontal plane is perpendicular to this, and of course the sagittal plane is in the midline. Roentgenograms are first taken with the stereoecephalotome in place, and calculations are made, taking into consideration the enlargement of the image of the skull on the film, so that the needle can be advanced to the desired location. This makes possible the approach from oblique angles with the same accuracy as if the needle were introduced vertically. At operation the instrument is applied in the exact location on the scalp where the original roentgenographic studies were made, and the needle advanced to the desired location. The coagulating current is turned on for the appropriate time, then turned off, and a drop of iodized oil injected. The procedure seems quite benign, although the period of operation is necessarily a long one.

The body of the book contains a stereotaxic atlas of the brain which can be used for proper location of the various structures that are considered for approach. A cellophane grid is supplied, so that the reader may locate any desired structure in terms of the zero point. Thus the red nucleus lies 15 mm. anterior to the center of the pineal gland (approximately the posterior commissure), 10 mm. below, and 5 mm. laterally. Illustrations of Weigert-stained material are also present, but show the degree of shrinkage. A study of variability was made, using 30 brains, and compared with somewhat similar measurements made upon roentgenograms. (The data are presented in 31 tables.) The variations were further checked by postoperative roentgenographic studies, and in only one case in 20 was there a deviation of more than 1.8 mm. from the intended spot. The final proof was available in a patient coming to necropsy 2 years after operation, whose brain showed excellent symmetry of the electrolytic lesions. In addition to lesions placed in the thalami for relief of mental disorders, the method was tried unilaterally on the substantia nigra in a case of hemiballism, and on the spinothalamic pathway in the diencephalon in a pain case. The postmortem sections reveal how close the lesions were placed to the target point. The authors go on to state: "However, it cannot be emphasized too strongly that satisfactory results can be expected only if one scrupulously adheres to the details of the technic described in previous chapters, particularly the exact reapplication of the SET [stereoecephalotome] at operation. Otherwise, disappointments and failures are bound to occur that may be disastrous."

Only those who have attempted similar precise work can really appreciate the difficulties involved in placing minute lesions at such distances from the periphery of the head. The pitfalls are numerous, the apparatus cumbersome, the patients variable and possibly, even probably, unreliable. The cerebral tissue is by no means a simple colloidal mass, but is made up of gray matter and systems of fibers of varying density, and the latter may lie parallel to the track of the inserted needle, and yet lead that needle astray. Research has shown that the cells of origin of many of the pathways within the

brain lie in the gray nuclei near the base. Therefore it seems reasonable to investigate those nuclei in the most accurate fashion possible, while maintaining an alert eye for the patients' responses. This work is a refinement of psychosurgery that may lead to greater understanding of the mechanisms of brain, mind, personality, emotion, and the spirit. It is not too much to hope for that these investigations may show the way toward more effective treatment of the mentally ill. While other methods are stressing the practical application of anatomy and physiology to the problems of the sick individual, this intricate research may well prove that much of present-day psychosurgery is clumsy, even bungling. It is to be hoped that in future parts of this projected monograph, some new answers will be laid down for us to think and argue about.

WALTER FREEMAN, M.D.,
Los Altos, Calif.

SPINAL NEURINOMA. A CLINICAL STUDY OF 44 CASES. By *Bendt Broager*. *Acta Psychiatrica et Neurologica Scandinavica, Supplementum No. 85.* (Copenhagen: Ejnar Munksgaard, 1953.)

This is a valuable, detailed study which will be of service to the neurologist, the neuropathologist, and the neuroradiologist, as well as to the neurosurgeon.

Each section of the monograph is well summarized and the illustrations and tables are good. Individual records of the 44 cases, and a bibliography of 229 articles are included at the end of the text.

The cases were drawn from the author's experience with 271 microscopically verified spinal tumors. The monograph deals mainly with the clinical differential diagnosis of these 44 neurinomas (neurofibromata), from 86 spinal meningiomas and 43 intramedullary spinal gliomas.

Dr. Broager has followed 28 of his patients for periods of 2-16 years. He classifies the result of operative removal of the tumor as good or fairly good in 30 of his 44 cases.

ERIC A. LINELL, M.D.,
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MAN'S CAPACITY TO REPRODUCE. By *Joseph W. Eaton and Albert J. Mayer*. (Glencoe, Ill.: The Free Press, 1952. Price: \$2.00.)

The Hutterites are an Anabaptist religious group living in the United States in the Dakotas and Montana and in Canada in Manitoba and Alberta. They live in colonies of approximately 100 people and "swarm" to a new area and establish new colonies when the number reaches a level much above this. Their sect does not believe in individual ownership of property; all land, machinery, houses, furniture, clothing, and food belong to the colony, not the family. All eat together in a common dining room; no cooking is done in the individual homes. There is limitation on education and life is

primarily agricultural, but the most modern machines and techniques of farming are used. Although research has not upheld the claim, the sect has long had a reputation for having very low rates of mental illness and appears to show low rates of crime and of marital conflict. The sect originated in Switzerland in 1528, migrated to Russia, where it fell to low membership, and finally to the U. S. in 1870. The sect does not believe in limiting births after marriage, but the beginning of reproduction is delayed by the belief that adult baptism must be accomplished before marriage takes place. The average age at marriage for females was 22.0 and for males, 23.5 in 1950 with little evidence of change since 1880.

In 1880 there were 443 Hutterites in the U. S. In 1950 there were 8,542, representing an increase in population of about 4% per year, and a doubling of the population every 16 years. This is the highest reproduction rate known for any human group and the authors feel that it is about the maximum the human race is capable of. There has been little migration out of the sect and little proselytizing so that these factors do not markedly influence the reproduction pattern.

In general, health is at a fairly high level. Infant mortality and death rates of children up to 14 years are somewhat higher than for the general population; this may be due to the general use of midwives and to the fact that the sect must use "outside" physicians and may delay too long in calling on them for service. An unusual feature is that there are more men than women in the older age groups of the population; it is suggested that this may be due to damage of the health of the women through excessive childbearing.

The history of the growth of Hutterite populations is compared with a few others and its unique features are pointed out. There is as yet no evidence that the rate of population growth is falling, though the authors suspect that this may take place in coming generations since they found some complaining on the part of the women and the possibilities of birth control are known to the population.

This study is a part of a much larger study of the sect, particularly in relation to the incidence of psychiatric diseases. The study when complete in all its facets will certainly be one of the most significant anthropological investigations extant.

PAUL V. LEMKAU, M. D.,
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School of Hygiene and Public Health.

MANIC-DEPRESSIVE DISEASE: Clinical and Psychiatric Significance. By John D. Campbell, M. D. (Philadelphia: Lippincott, 1953. Price: \$6.75.)

The author of this volume has treated his subject most thoroughly. It is well documented with references and he has used Kraepelin and Kraepelin's contemporaries as the foundation in developing his subject. The text is couched in simple language so that it should appeal to the nonpsychiatrist, and demonstrates that we do not require a new vocabulary to present a psychiatric subject.

Throughout the text there are frequent discussions comparing the psychoanalytical and the psychobiological interpretation of the various phases and factors of this disease, and the author has utilized the writings of authorities in both of these fields of psychiatric thought to point up such comparisons.

The description of his subject has been particularly thorough and the only criticism which might be offered is that probably some of the features described as characteristic of manic-depressive disorder are too general in their occurrence in disease to contribute significantly to the separation of the manic-depressive picture from allied conditions. The feelings of unreality or depersonalization described as an autonomic dysfunction would suggest that the author is discussing a schizo-affective disorder. There does not appear to be any significant consideration given this mixed type of psychiatric illness. It also might be a little difficult for some readers to understand the meaning intended by the heading "Autonomic Disturbances of the Cranium," but on reading this section one finds that the author refers to the cranialgia that sometimes accompanies a manic-depressive episode. There is an excellent chapter on the differential diagnosis of manic-depressive disease, followed by a chapter giving practical consideration to the social maladjustments of the manic-depressive.

The final chapter makes a survey of the physical therapies now in vogue in the treatment of this condition and, as throughout the rest of the book, the author relies on reports from authoritative sources to assess the relative merits of and indications for these therapies.

This volume should be of real value to the general practitioner, an excellent book for the resident in training in neurology and psychiatry, and profitable reading for the practicing psychiatrist.

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FACTORS AFFECTING COSTS OF HOSPITAL CARE.

Edited by John H. Hayes. (Toronto and New York: The Blakiston Company, 1954. Price: \$4.00.)

Since 1948, most general hospitals have been free of deficits. This has occurred in spite of the fact that hospital expenditures have increased 200% in the past 15 years. The prosperity of hospitals is due chiefly to increasing occupancy ratios, so that there is very little waste space and few unused facilities.

This book is the first report of the Committee on Financing Hospital Care sponsored by the American Hospital Association and several foundations. It is a hospital-oriented, rather than a patient-oriented or doctor-oriented, report. For example, it suggests that hospitals take more responsibility for general community health, that they develop home care programs, that they offer more in-building facilities for the private care of ambulatory patients, and that they encourage Blue Cross

to cover outpatient as well as inpatient service. All these things will, of course, expand the hospital empire. What they will do to private practice sends chills up and down the spines of many private practitioners. Or, as a second example, it points out that one way of decreasing expenditures (already well below income in most hospitals) is to police the doctors more closely so that they do better work-ups prior to admission, double-check the usefulness of a laboratory test before ordering it, and stand ready to discontinue a drug or physiotherapeutic procedure as soon as possible. The report, indeed, says bluntly that some doctors order tests "merely because costs are covered by insurance."

There is no index entry under "mental hygiene" or "psychiatry." One wonders whether the report writer knows that no institution can be a truly "general" hospital if it fails to provide some psychiatric care, at least for acute or short-term mental illness. Someone ought to tell him.

HENRY A. DAVIDSON, M.D.,
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THE PSYCHOLOGICAL VARIABLES IN HUMAN CANCER. A SYMPOSIUM. Edited by *Joseph A. Gengerelli and Frank J. Kirkner*. (Berkeley and Los Angeles: University of California Press; London: Cambridge University Press, 1954. Price: \$3.00.)

Herein are the presentations and discussions thereon of some clinical impressions and psychological findings in patients with advanced cancer. The number of patients subjected to the psychological "tests" was small but the statistical analysis of the findings is supposed, apparently, to overcome this difficulty and to obviate the need for other rational considerations regarding the quality of the primary data and their significance. The psychological data thus treated tend to support the clinical impression that slow-growing cancers are likely to be found, though not exclusively, in emotionally dull, and fast-growing cancers in emotionally sharp, individuals. In the discussion of these findings, clinicians of high standing in medicine, surgery, and psychiatry challenge their validity if they do not entirely counter them.

While no competent clinician would deny that there may be some relationship between the emotional make-up of the individual, or what determines it, and cancer(s), (etiology or progress), it is doubtful that any clinician will find here anything that will convince him of such relationship or help him crystallize his opinions in that regard. The presentation of the psychological data, marked with enthusiasm as it is, is not likely to reduce the gap between clinical medicine and modern psychology, or stimulate the much needed study of the relationship between mind and body. As implied in some of the discussions, it would have been better if there had been many more observations and much more rational consideration—the best test for significance—and less, and less need for, extensive and hazardous statistical analysis.

NEIL MCKINNON, M.D.,
University of Toronto.

A SPECULATION IN REALITY. By *Irving F. Laucks*. (New York: Philosophical Library, 1953. Price: \$3.75.)

This work presents certain facts in the physical and biological sciences, a physical hypothesis to explain paranormal psychological phenomena (extra-sensory perception, etc.), and some speculations in favor of the existence of the human "soul" and an afterlife. It is an engaging book, simply written, without cumbersome terminology. The author obviously tries to cover an encyclopedic range of scientific phenomena and philosophical speculation. The approach is authoritative in some cases but perhaps lacks an adequately critical viewpoint in the sections dealing with paranormal phenomena.

The first 4 chapters deal with such topics as modern concepts of atomic nuclei, ordinary chemical reactions with particular reference to properties of protein molecules, relationship between chemical phenomena and life, and what the author terms various activities of energy. Chapter 5 deals with biological evolution and Chapter 6 with instincts, both in relation to chemical reactions. The final 3 chapters are more highly speculative, dealing with the concept of soul which the author accepts in a dualistic framework. The reality of occurrence of all types of paranormal phenomena is accepted as truth without reference to the highly controversial aspects of this vexing field. These paranormal phenomena include the various performances of mediums, mental telepathy, clairvoyance, psychokinesis, and materialization. The author's explanation of these phenomena is the hypothesis of "A-rays" which join brain and soul; both brain and soul are broadcasters and receivers of "A-rays." It is noteworthy that some of the leading experimentalists in parapsychology reject such physical explanations of their results and lean toward purely "mentalistic" explanations.

To this reviewer, the principal value of this work lies in its exposition for the lay reader of certain facts of the physical and biological sciences, which are available, however, in numerous other excellent presentations. The more speculative portions suffer from lack of truly critical analysis.

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LOBOTOMY. A CLINICAL STUDY. By *A. Miller*. (Toronto: Ontario Dept. of Health. 1954.)

Teamwork in the field of psychosurgery has become practically a necessity when any large study is undertaken. In this monograph the experience of the staff of the Toronto Psychiatric Hospital during the years 1948 to 1952 has been brought together in a single volume replete with tables and colored charts that answer many questions concerning prefrontal lobotomy. The choice of patients has been outstanding, since although practically all of them were considered hopeless, chronic, and difficult, nevertheless, after operation two-thirds of the patients were out of hospital, and 55% of all patients were functioning effectively. Point (d) in the selection of patients probably explains as nearly as possible the superior results in this study: "The

patient should present clinical features which, in the light of clinical experience gleaned from other sources and our own experience, could reasonably be influenced in a beneficial way by lobotomy treatment."

But this study contains much more than a simple recitation of clinical results in lobotomy. It aims at determining in advance the results of surgical treatment. The methods are many and various, but: "For practical purposes, it can be said that the predictive assessment was good in . . . 48%." This is not high enough to please the clinician. Study of the accompanying chart shows 2 things: first, that operative complications are serious deterrents to good results, and, secondly, that prediction has not notably improved in the 5 years covered by the study.

A point system has been used for grading the patients before and after lobotomy which seems quite clear-cut as far as the social adaptability of the patient is concerned. It is less concerned with the intricacies of psychologic reaction. The half-way mark is attained by a patient who is out of the hospital, not supervised, yet not working. The zero point is that at which the patient is a nursing problem, and the 100-point level sees the patient intellectually, socially, and emotionally normal, and working normally. Many factors making for good or poor adjustment after lobotomy are presented. The author comes to the conclusion that the duration of illness is not an important factor. However, since practically all the patients had been ill for 5 years or more, this statistic must be looked upon with suspicion. On the other hand, the effect of deterioration in defeating the purpose of operation is all too evident. Preoperative shock treatment with good though temporary response is a good sign. The marked superiority of the affective and psychoneurotic types in comparison with the schizophrenic types shows up well in this study.

Many special clinical and laboratory studies are included in the monograph. Of interest is the fact that slow occipital alpha rhythms were found preoperatively in greater number among the improved patients. Postoperatively, the incidence of alpha rhythm was definitely increased. High glucose tolerance curves found in anxious subjects tended to become lower after operation. Psychometric and psychologic tests showed variable effects, with rather low predictive value. Illustrative case reports complete this handsomely printed monograph.

WALTER FREEMAN, M.D.,
Los Altos, Calif.

THE MANAGEMENT OF MENTAL DEFICIENCY IN CHILDREN. By *I. Newton Kugelmann*. (New York: Grune & Stratton, 1954. Price: \$6.75; Toronto: Ryerson, 1954. Price: \$7.00.)

The author gives as the purpose of his book "to reveal the mechanism and management of mental deficiency in infants and children." He accomplishes this by dividing his work into 3 parts: Part I—Diagnosis; Part II—Syndromes; and Part III—Management.

In Part I he briefly sketches history, concepts, and clinical classifications of mental deficiency in children. It is obvious that he does not intend to deal with these subjects exhaustively since each one draws a volume in its own weight. Sufficient references are given to enable the reader to pursue these subjects further if desired.

The remainder of Part I is devoted to "The Complete Examination of the Retarded Child." Etiology, history, physical examination, functional examination, and the mental examination receive quite complete attention. Although the author directs his attention toward the parents and discusses some of the pitfalls to be watched for in obtaining a history from the parents, the reviewer would have preferred that more attention be paid to the parent-child relationship, possible effects of emotional deprivation, and evidence of unhealthy attitudes which would have a detrimental effect on the child. The remainder of this section is complete and quite satisfactory.

In Part II, the author has classified the childhood amenities into 4 groups of related syndromes: developmental, metabolic, neuromotor, and psychological varieties, which are further subdivided by outstanding symptoms. He has successfully presented a clear, workable, and concise outline which adequately covers the field and should be of utmost value to the new student in this particular field. In fact, if this book accomplishes nothing more, and it does, this one section would be an outstanding contribution. The outline provides a most effective guide to diagnosis. The author refers to Morquio's disease and states that there is no intellectual defect. The reviewer has reported a brother and sister with Morquio's disease having moderately severe mental retardation.

Part III, Management of the Retarded Child, deals with training, education, treatment, and prevention. Many practical suggestions are found in this section. The section on preparing the parents is excellent, as are those on training of the child. While the section on education is brief it contains valuable information. However, little attention is paid to facilities or programs for the trainable group as compared with the educable children. The section on treatment is all too brief. Some mention is made of the value and the need for psychotherapy for emotional disturbances in the retarded. The reviewer feels that consideration should be given to psychotherapy, both individual and group, in a more comprehensive manner in this section.

There are many who will take exception to the statement that "a severe ament of I. Q. about 25 should be institutionalized at birth or before the fifth year." Two paragraphs later the author states "an infant ament needs home care for security, affection and attention of his parents and family." There is much evidence to show that a child may suffer emotional and intellectual impairment when he is institutionalized early and experiences emotional deprivation. This is in accord with the WHO report on the retarded child. Then, too, one must admit that psychometric levels at birth and during the first few years of life are

not accurate in the least and should not be utilized in themselves for purposes of prognostication or for making the serious decision of institutionalization. This first statement seems to contradict the author's own words when he says that the book is "dedicated to the inalienable right of every child to the full development of his physical, mental, emotional and social potentialities. . . ." Institutionalization must be decided only after careful evaluation of the needs of the child and the family.

In spite of the above the section on Treatment contains many valuable suggestions, particularly for parents, in managing the everyday problems which arise in the handling of the retarded child.

The section on Prevention is exceptionally well handled. The discussion on eugenics is sound except as noted below, as is that on prenatal care, parental age, dietary, endocrine infectious disease, and other disorders on the part of the mother. The importance of the natal and postnatal periods is well handled.

Many authorities will disagree that "Hereditary disorders produce seventy per cent of the aments." There are many, including the reviewer, who feel that as more scientific knowledge is accumulated, and evidence is compiled, more conditions will be taken out of the hereditary group.

Generally speaking the bibliography is well selected and complete. It would be more valuable to the student and others if the references were annotated with the text and, where authors and investigators are mentioned in the text, that the complete reference be given.

In spite of the above criticisms the author has made a distinct and valuable contribution to the literature in this field. His dynamic approach to the problem is praiseworthy and should point to the need for contributions in this field by dynamic psychiatry and its concepts. This book will be of great value to psychiatrists, especially those dealing with children, and to pediatricians, psychologists, social workers, teachers, and others called on to give advice and guidance to distraught parents of retarded children.

MALCOLM J. FARRELL, M. D.,
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THE PERMANENT REVOLUTION IN SCIENCE. By Richard L. Schanck. (New York: Philosophical Library, 1954. Price: \$3.00.)

The Institute of Experimental Method is an organization of the students of Edgar Singer devoted to the task of establishing methodology as a science. They hope thereby to wean from philosophy, the mother of the sciences, what they regard as the last of her offspring and to leave her with no further useful functions. The author of *The Permanent Revolution in Science* is a member of this group, concerned in the present case to indicate the emergence of a new and revolutionary approach in the method of the sciences. His book is at once a history of the events in the revolution and an advocacy of the extension of its principles. The most important feature of the revolution is a shift from concern with the individual thing, taken as an element of scientific inquiry, to concern with the

society or system as the element—"a system of trends, effects, waves, or other stable statistical relationships." The notion of trends reintroduces teleology into science, but a teleology purified of the "animism" of Aristotle. He examines in turn each of the sciences of physics, chemistry, biology, psychology, sociology, and ethics in the light of his general thesis. The most interesting section is, perhaps, that on psychology, in which Freud's psychoanalytical approach to personality is given an illuminating interpretation in terms of the thesis. The least satisfactory section, though the most important in purport, is that on ethics. It is far too brief to do justice to the complexity of the problem. Just because ethics has not historically been established as a science in the sense in which physics or chemistry is a science, the problem of method in ethics is not only more complicated but is different in nature. In an established science there is already a methodology implicit in the procedures of the scientist which is there for inspection. It is the methodologist's business in such cases to make the scientist self-conscious in what he is doing. It is just such a task of inspection that the author has been engaged upon in the first chapters of his book. But in ethics, which is not yet a science in the way that physics is—and one may be sure that if that unlikely event ever takes place the world will hear about it—the methodologist has not got similar data on which to work, and his problem is consequently of a different nature. It is not sufficient to say that what remains to be done is to extend the methods found in "science" to ethics, for what, after all, is the subject matter that one is claiming to extend this method to? It is unlikely that many readers will be able to get off to a start with the same set of unmentioned assumptions about it as those contained in Professor Schanck's 12 brief pages devoted to ethics.

One must protest against the perpetuation in the opening part of this book of the myth that it was experiment that gave rise to modern science. There is no longer excuse for historians of science to keep repeating that favorite but unfounded story about Galileo and the tower of Pisa. Far from it being the case that Copernicus "laid the foundations of modern attitudes toward experimental science," there is not a better example than Copernicus' of a scientific revolution which occurred wholly independently of any experimentation. The empirical facts available to Copernicus were simply those which he accepted from Ptolemaic astronomers, and those empirical facts gave greater support to their theory than to his. But Copernicus had the courage, shared later by Galileo, which is required for sticking to a theory in spite of the observed facts. It is to such courage that science owes some of its most important advances. As for Newton's *Principia* as representing the triumph of the experimental method, surely it represents a brilliant triumph in synthesizing what had already been established piecemeal, rather than in formulating laws through experimentation.

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ANNUAL INDEX

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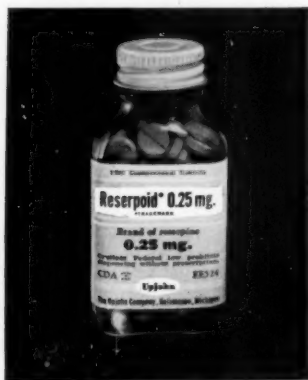
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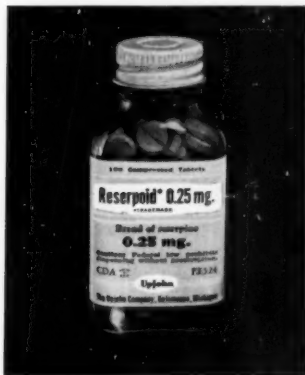
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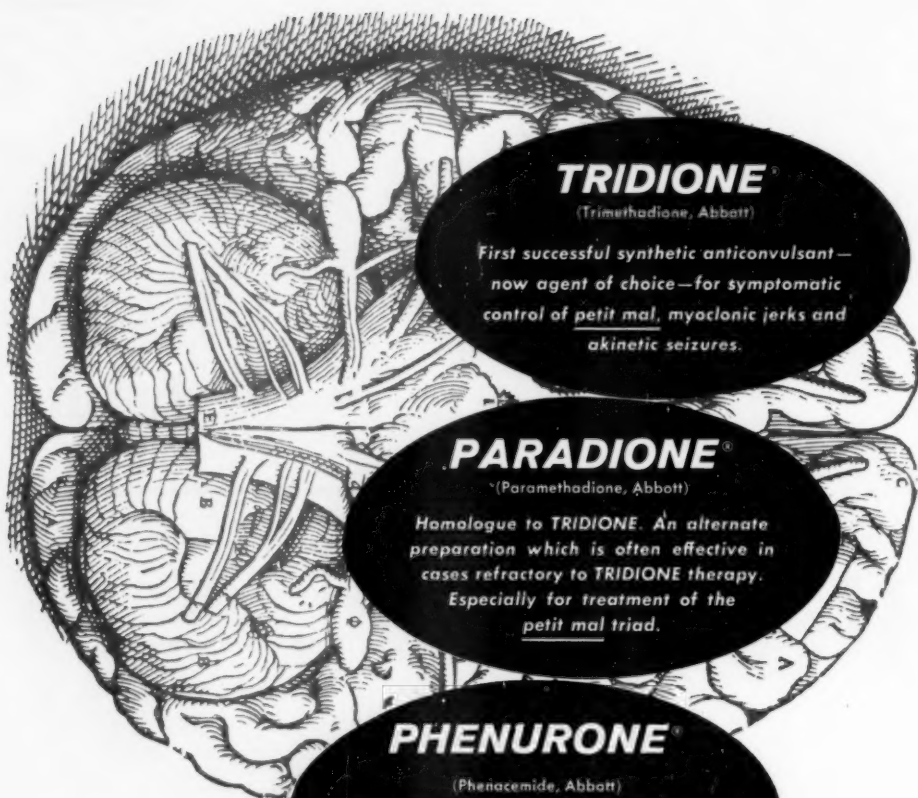
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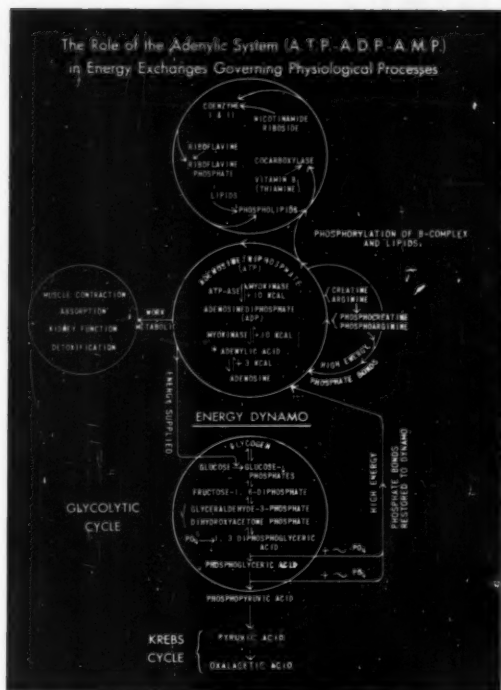
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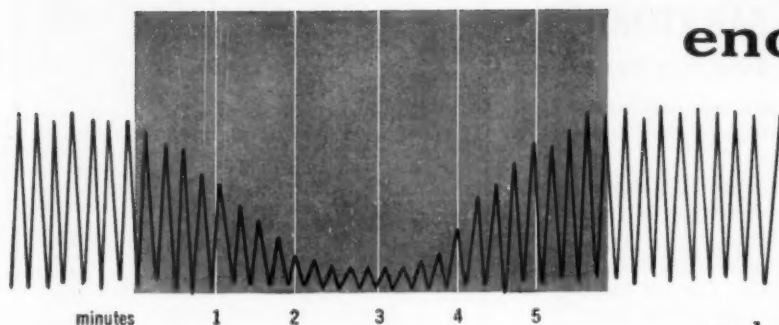
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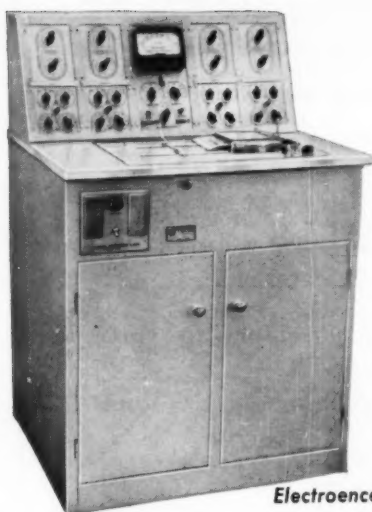
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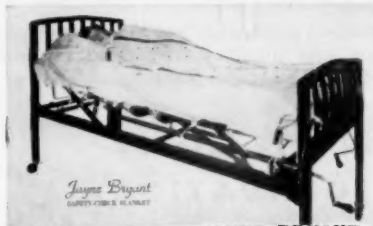
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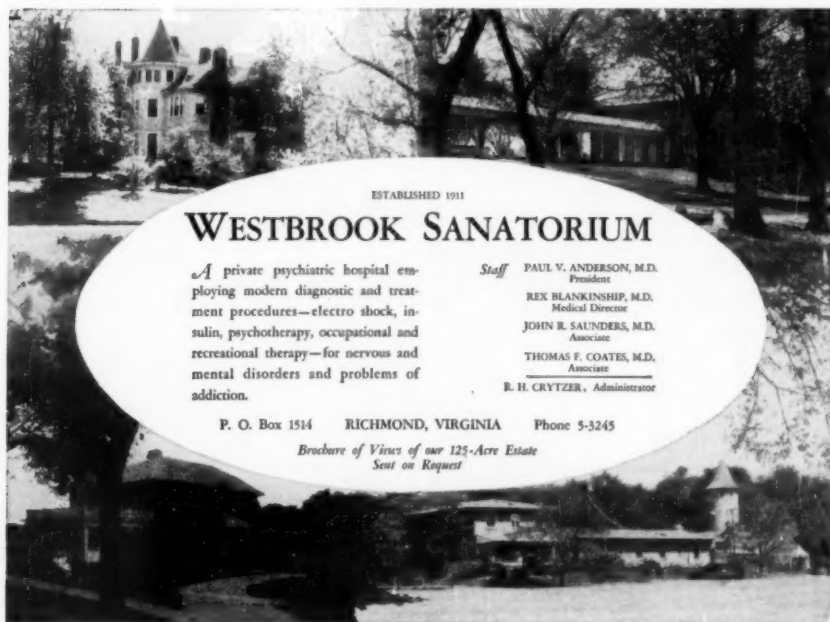
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